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PAGET'S DISEASE OF BONE (OSTEITIS DEFORMANS)

A Review of 48 Cases

B. H. NICHOLS, M.D., and J. R. RAINES, M.D.

It is now more than sixty years since Sir James Paget[1] described the bone disease which bears his name. He advocated the term "osteitis deformans", but this would seem to be a misnomer. We do not believe infection to be concerned in the cause, and we know that in many cases there is no skeletal deformity. Therefore, we prefer to designate it "Paget's disease". A summary of the salient features encountered and the present-day concepts of the disease, together with a review of 48 cases recorded at the Cleveland Clinic, are presented.

The advanced stages present a striking picture of skeletal changes, and the classic cases with the massive but well-formed head, reduced stature with marked kyphosis, the great anterior bowing of the legs and the pendulous abdomen present no difficulty in diagnosis. These cases are uncommon and the frequently diagnosed ones are much less advanced, perhaps involving but one bone. It is in these early or localized lesions that the differential diagnosis becomes more formidable and important.

INCIDENCE AND DISTRIBUTION

Paget's disease is frequently recognized now. Brailsford[2] was able to collect only 300 cases which had been recorded prior to 1926. He added 154 cases of his own in 1936 and since that time many others have been reported. Forty-eight cases have been diagnosed and recorded at the Cleveland Clinic.

Paget's disease is essentially a disease of late life, perhaps later than the average carcinoma age, although in most cases the disease has been present some years before it is recognized. The average age in our series was about 60 years; the youngest was 32 and the oldest was 88 years of age (Table 1). No important difference in sex incidence was shown, this series consisting of 15 women and 33 men. All were white, although the disease may occur in Negroes. One patient reported two siblings with a definite diagnosis of Paget's disease, a familial tendency that has been seen frequently. Several cases have been described in children, but they do not seem to be well authenticated.

TABLE 1

Age Distribution

30-40	*40-50*	*50-60*	*60-70*	*70-80*	*81*	*88*
2	6	18	18	2	1	1

Schmorl[3], in the course of his work on intervertebral discs, became interested in Paget's disease and made complete skeletal examinations on 4,600 persons. He made a diagnosis of Paget's disease in 138 of these cases, an incidence of 3 per cent in persons past 40 years of age. The greatest number of lesions was in the spine, including the sacrum. However, many of the lesions were local, some being almost microscopic and obviously nonclinical. Thus, the relative distribution in the skeletal system seems to depend somewhat upon the method of diagnosis used.

It has long been said that the skull and femur are the sites of greatest predilection; however, later authors place the spine and pelvis first. Table 2 lists the frequency with which various bones were involved, as well as the number of times that the involved bone was radiographed in the series. Some patients had only one or two bones radiographed so that involvement elsewhere can only be conjectured. In other cases only portions of the spine were examined. Obviously, full skeleton radiographs of each patient would be required to determine the true distribution. The tendency for routine abdominal radiographs on gastrointestinal and genitourinary cases probably has led to the finding of a disproportionate incidence in the pelvis and lower spine, although Schmorl reported a similar incidence.

TABLE 2

	Frequency of bone involvement (by radiograph)	*Number of times radiographed (all or part)*
Skull	18	27
Spine (or portion)	16	39
Pelvis	35	39
Femur	18	27
Tibia	11	13
Forearm	3	4
Humerus	5	6
Metacarpal	1	1
Scapula	1	1

A correct clinical diagnosis was made on the basis of the history and physical findings in 15 of the cases. In 9 others the radiologic findings of Paget's bones apparently were related to the presenting symptoms;

in the remaining 24 cases the diagnosis was made incidentally from changes seen in roentgenograms taken to investigate complaints aside from the skeletal system. There was no obvious constancy to this group of complaints. The typical symptom of the disease was pain in the back and legs, present for several years, with no particular aggravating or alleviating factors. When the tibia had been involved, many patients noticed anterior bowing of the leg. Only a few of the 17 cases with skull involvement had noticed enlargement of the head. One case with multiple involvement but normal skull radiographs complained of increasing hat size. Two cases presented themselves with fractures of involved bone.

ETIOLOGY

No theory of the cause of this enigmatic disease thus far advanced has gained wide acceptance. Paget considered it an inflammation of bone, but this idea is thought to be untenable at present. Moller[4] pointed out the similarity of chronic fluoride intoxication, but important differences are present. In fluoride poisoning the bone changes are symmetrical, universal, and slowly but surely progressive, while Paget's bones are asymmetrical and unpredictable in their progression.

Great efforts have been made in the past to incriminate endocrine factors, particularly dysfunction of the parathyroid glands. This view has been partially abandoned and, according to Jaffe[5], no case of a parathyroid adenoma associated with Paget's disease has been reported since 1926. Three of our cases had parathyroidectomies. All had normal glands and had only temporary relief of symptoms. Adrenal cortical extract has been reported as a successful therapeutic agent, although there is no obvious logical basis for it[6]. Jaffe believes that this is not a systemic disease and therefore is less apt to be a metabolic disease. He feels that it may be a breakdown of the normal mechanism for replacement of bone.

Moehlig and associates[7] pointed out a familial tendency to obesity, tallness, and diabetes in a series of their patients. These cases showed an elevation of the glucose tolerance curve and a high carbohydrate diet with insulin relieved their pain. One of our cases had a diagnosis of chronic hypoglycemia, but no diabetic cases were encountered.

Trauma has been cited as a factor. However, in at least some of these cases bone changes were shown to be present before the trauma. European writers speak of "pagetoid" bone disease following trauma. With a typical monostotic lesion this terminology would seem more discreet. One of our monostotic cases gave a history of trauma, and the roentgenologic changes were typical.

In our cases both serum phosphorus and calcium levels were at the upper limit of normal. The mean serum calcium reading was 10.8 mg.

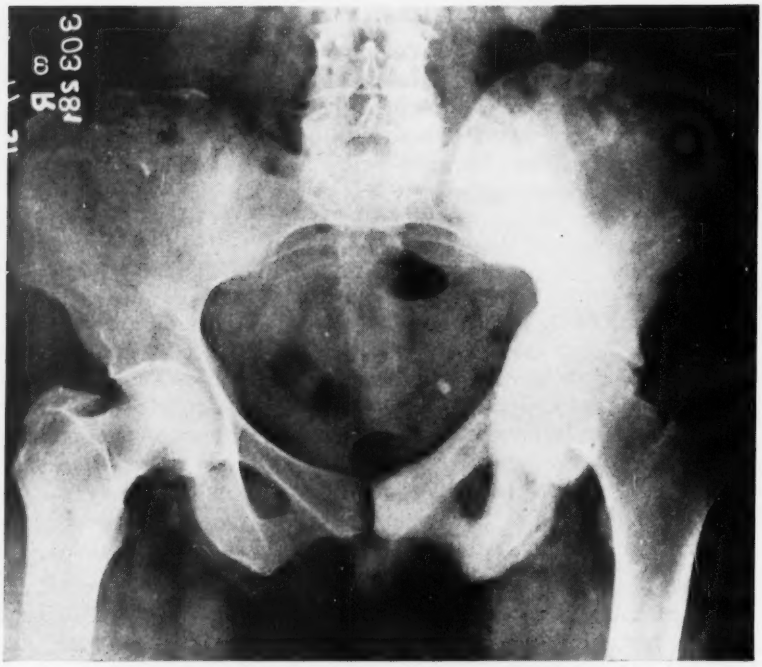

Figure 1: Paget's osteitis deformans with typical thickening and sclerosis, and with unilateral distribution.

per cent, with normal figures being 9 to 11. The average serum phosphorus was 3.7 mg. per cent, and normal is 2 to 4.0. The highest calcium reading was 11.7 except in a case which was suspected but not proved to also have hyperparathyroidism, and the highest phosphorus, 4.2. The literature indicates that the serum calcium usually is somewhat low, but such was not the case in our group. In osteitis fibrosa cystica the serum calcium is definitely elevated and the serum low.

The only constant laboratory finding is the marked elevation of serum phosphatase activity, which reaches its highest levels in Paget's Disease. It may rise to 80 units or more as contrasted with a normal maximum of 4.0 by the Bodansky method. There is some correlation between the activity and extent of the disease and the phosphatase level. Certain other diseases give moderate phosphatase elevations. These include osteitis fibrosa cystica, rickets, bone metastases from carcinoma of the prostate[8], and certain liver diseases with jaundice. Destructive bone lesions are less apt to have elevated serum phosphatase values.

Thus far we have discussed the commonly employed "alkaline" serum phosphatase determinations. Kutscher[9] has described phosphatase

readings done on acidified serum in which by far the highest levels are found in patients with bone metastases from carcinoma of the prostate. He calls this substance prostatophosphatase. Gutman[8] finds that in Paget's disease this "acid" phosphatase is normal in nearly all early and moderately advanced cases. This may represent a valuable differential procedure in certain cases.

PATHOLOGY

The sequence of pathological changes in the bone in Paget's disease has been well determined. There is primarily a progressive absorption of bone with accompanying osteoporosis and vascular changes, followed by the laying down of new bone, or one might better say osteoid tissue because little attempt is made to reproduce normal bone structure. Early in the disease the bone is quite soft, and it is at this stage that bowing of the long bones begins, due probably to muscle pull. With expansion of the bone this may continue, especially in the leg and forearm, because of inequality of length when the adjoining bone remains normal. A considerable amount of fibrous tissue is formed, which may almost obliterate the marrow cavity. This tissue is vascular and osteoblastic. Most of the bone is deposited from the periosteum.

The typical end picture is a longer bone, laid down on a more porous plan. The trabeculae are coarse and the fragments of lamellar

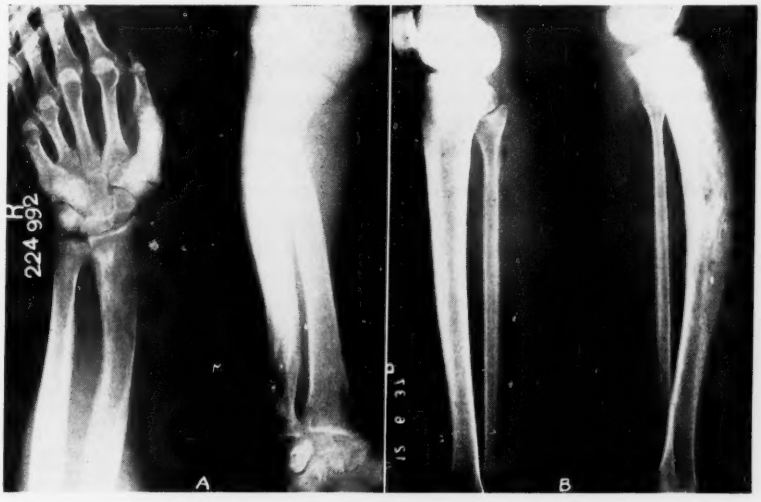

FIGURE 2: A. Involvement of left ulna, right first metacarpal and right radius showing varied distribution of Paget's disease in the long bones.

B. Thirty-nine year old woman with bowing and enlargement of leg following trauma, with characteristic changes.

bone are laid down as an irregular mosaic with little evidence of recreation of the haversian systems. This distinguishes the disease pathologically from any other bone disease. The irregular mosaic pattern was Schmorl's criterion for the diagnosis of Paget's disease.

Vascular changes are seen particularly in the skull. The vessels show thrombosis, congestion, hemorrhage, and edema. Some feel that it is primarily a vascular disease. Large areas of hemorrhage or anemia with necrosis result in the appearance of pseudocysts which are frequent. The varied pictures seen roentgenographically depend upon the stage of absorption and redeposition of calcium at the time. This process characteristically may be arrested in any stage with minimal involvement, or it may "spread" to involve many bones.

ROENTGENOLOGIC FINDINGS

The well known typical roentgenologic picture is one of altered density in bone. There is first a porosis with the resorption of bone, followed by a widespread sclerosis and increase in bone size, with loss of the normal structure. This may vary, depending upon the type of bone involved. The shaft of the long bones often is curved and the entire bone becomes greater in diameter. There is loss of normal cortex shadows and the appearance of a much thickened, not entirely regular cortex, less dense in some regions and more dense than normal in others. There may be small areas of decreased density suggestive of cysts. The entire bone usually is not involved, and the demarcation between normal and diseased bone is fairly sharp and often V-shaped. The epiphysis offers no barrier, a fact which is a valuable differential point. The marrow cavity is narrowed, and the trabeculae, especially at the ends, are thickened and irregular. The bone as a whole is less dense than normal until late in the disease and may have the appearance of cotton wool.

The skull is thickened, and the tables are not distinguishable. There are very typical mixed areas of porosis, with numerous small circular areas of greatly increased density representing localized sclerosis. The outer table and diploe show the first and greatest involvement. Some early cases show large well-defined areas of uniformly decreased density which is termed osteoporosis circumscripta, and which has been described by Kasabach and Dyke[10] and others as a progenitor of Paget's disease with the usual train of Paget's changes following it. We have not recognized a true osteoporosis circumscripta.

When the pelvis is involved the radiographic picture is often one of widespread, dense, but not uniform sclerosis with some areas of decreased density. The increase in diameter aids to differentiate it from osteoblastic metastases, such as from carcinoma of the prostate. The uniformity of the lesion in metastases is also notable.

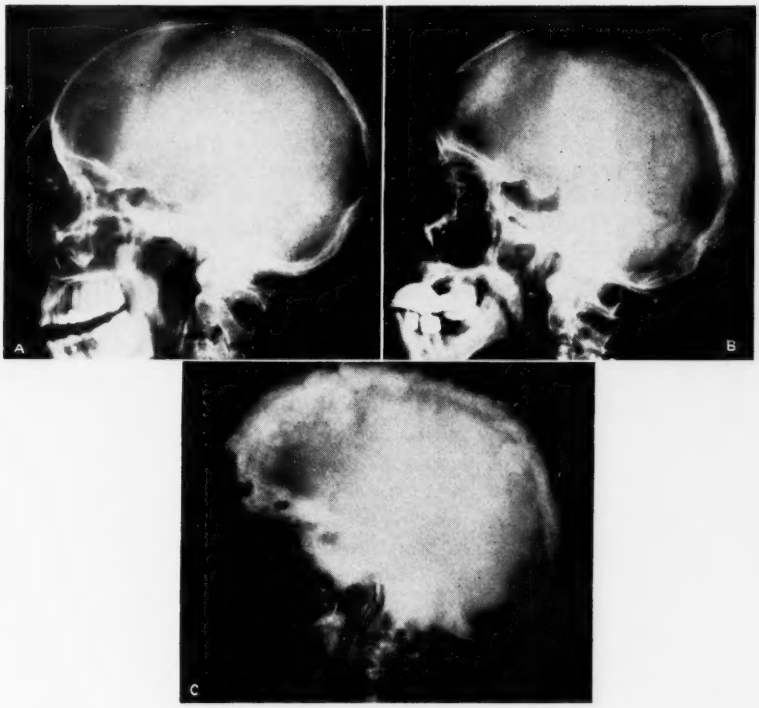

FIGURE 3: We believe these three cases represent stages in the development of Paget's disease.

A. Early changes with osteoporosis and thickening of the calvarium. The pelvis showed typical findings.

B. There is extensive involvement with mottling, thickening, and osteoporosis. There was no increase in hat size.

C. Typical advanced changes.

The spine usually shows dense, irregular, wavy trabeculae. The vertebral bodies may cause cord compression by collapse or increase in size. Usually the entire vertebral body is more or less evenly involved, and one or several may be affected. If more than one is involved, they are usually adjoining ones. The increase in width may extend out beyond the intervertebral cartilages, and bony union may then occur.

Joints are involved rarely, but there may be apparent irregular superficial defects in the periosteum. Often an adjoining ilium and femur will be involved in unilateral disease without evidence of joint disturbance.

COMPLICATIONS

In Paget's bones there is a definite tendency toward the occurrence of fractures with minor trauma. These usually are transverse and are relatively painless[11]. A callus appears early and prompt healing occurs. Multiple transverse fissure fractures in long bones involved with Paget's disease have been described as possibly antecedent to complete fractures. Two of our cases were first seen because of fractures; one was of the forearm which occurred while driving a car, and one was of the scapula which resulted from a fall from a porch.

The relationship of malignant tumors of bone to this disease was noted by Paget in his first article, in which he described three bone tumors in his 7 cases. While the incidence is not nearly so high, there is an apparent connection between the two diseases. Coley and Sharp[12], in reviewing the osteogenic sarcomas listed in the American Registry of Bone Sarcomas, found that in 71 cases over 50 years of age, 28 per cent were in association with Paget's disease. In this group of cases the usual sites of predilection were involved, and in every instance the tumor was located in bone already the site of Paget's disease. Several had multiple points of origin, and the lesions were less radio-sensitive than in patients without Paget's disease. The newly formed osteoblastic marrow connective tissue seems to originate the tumor. In none of our cases was there an osteogenic sarcoma, and a review of all of our cases of osteogenic sarcomas in adults has shown no case of Paget's disease.

The occurrence of neurologic symptoms as a direct result of the bone changes in the skull is not well established. The auditory nerve in particular is thought to be encroached upon frequently. Several of our patients had varying degrees of deafness, and two had diagnoses of trigeminal neuralgia. Headache was a frequent symptom. Several cases of compression of the spinal cord occurring as a complication of Paget's disease in the spine and being relieved by laminectomy have been reported. Schwarz and Reback[13] reported this complication, showing how the increased size of the vertebral body encroaches upon the spinal canal and cord. These lesions are most often in the thoracic region, where the interpedicular measurements are smallest.

THERAPY

The wide range of therapeutic measures advocated by different workers bespeaks their lack of specificity. No clinical or roentgenologic cures have been reported, but symptomatic relief has been claimed from many measures.

Roentgen irradiation for pain, particularly of the long bones and spine, has been used frequently, and good symptomatic results have been reported[14].

Both parathyroid and adrenal extracts have been advised on empirical grounds. Watson[6] is especially optimistic about the use of adrenal cortical extract. We have used parathyroid extracts with doubtful benefit.

A high carbohydrate diet with insulin has been recommended[7].

Lineal osteotomy of long bones is said to be efficacious for intractable pain. Most logical is support or splinting, especially if the tibia is involved.

CONCLUSIONS

1. An analysis of 48 cases of Paget's disease of bone is presented.

2. No conclusions as to etiology have been reached.

3. Studies of serum calcium and phosphorus are mentioned, and the use of "acid" phosphatase activity measurements to differentiate metastasis from prostatic malignancy is suggested.

4. Roentgenographic differentiation between these two lesions can usually be readily made by the coarse mottling of the bone with alternate areas of increased and diminished density, increased size of the bone and bowing in Paget's disease. On the other hand metastatic prostatic lesions do not enlarge the bone but only show islands of increased density giving a mottled appearance of the bone. The location of the metastases usually is confined to the pelvis and lumbar spine, although occasionally other bones may be involved.

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THE LOCAL USE OF THE SULFONAMIDE DRUGS

GEORGE CRILE Jr., M.D.

Since the introduction of sulfanilamide and its derivatives, the reliance upon chemotherapy for the control of acute surgical infections has temporarily overshadowed the importance of sound surgical principles and often has resulted in the administration of inefficient or inadequate treatment. Too often, the physician fails to recognize the limitations of chemotherapy and vainly attempts to control the infection well beyond the optimum time for surgical intervention.

Chemotherapy is very effective in controlling infections from hemolytic streptococcus; is moderately effective in controlling staphylococcic infections; but is of slight value when administered systemically in patients infected with the nonhemolytic streptococcus or colon bacillus. However, even in infections caused by the hemolytic streptococcus or the staphylococcus, sulfanilamide and sulfathiazole cannot replace surgery after suppuration has taken place and mechanical drainage of an abscess is required. It is in the treatment of lymphangitis and cellulitis, not in the treatment of abscesses, that chemotherapy has been of the greatest value.

The work of Lockwood[1] and others has indicated that the products of proteolysis in vitro interfere with the bacteriostatic and bacteriocidal powers of sulfanilamide. The presence of similar substances in undrained abscess cavities probably interferes with the destruction of the organisms by chemotherapy. Accordingly, the sulfonamide drugs should supplement rather than replace early and adequate surgical drainage, especially in the presence of suppuration.

The local application of the sulfonamide drugs is based upon the principle that the local concentration of the drug in the tissues is ten to twenty times as high as that which can be obtained by any method of systemic administration. When high concentrations are reached, the drug becomes bacteriostatic for many organisms which are not affected by the oral administration of the same drug. Thus, the oral administration of sulfonamide has little or no effect upon a colon bacillus wound infection, but may reach effective concentrations in the infected tissues if the powder is sprinkled into the wound.

Since the popular acceptance of the local use of the sulfonamide drugs, a number of questions have arisen regarding the methods and the dangers of their use. The questions most frequently asked are: (1) What dangers attend the too rapid absorption and consequent overdosage of the drug? (2) Does a high concentration of the drug interfere with wound healing? (3) Are sulfathiozole or sulfapyridine more effective than the cheaper sulfanilamide in the treatment of infected wounds?

(4) Is it necessary to sterilize the drugs before applying them to clean wounds?

Question 1: Apparently there is little or no danger of overabsorption of the sulfonamide drugs when they are implanted in wounds or sprinkled upon raw surfaces. It is safe to state that the absorption of these drugs from wounds is invariably much less rapid than their absorption if equivalent amounts are given by mouth; and that much more of the drug can be safely implanted in wounds or sprinkled upon raw surfaces than can be given orally. Although 5 gms. or more of the powder has been used locally in wounds and upon raw surfaces, we have never seen the blood concentrations rise to levels higher than one-fifth of those obtained with similar amounts administered by mouth. The blood levels following local application of the drug in wounds or upon raw surfaces have not exceeded 2 mg. per cent.

When the sulfonamide drug is implanted in the peritoneal cavity, absorption may be more rapid than that following its application to wounds, but the blood levels still do not rise so fast or to levels so high as those following the oral administration of equivalent doses. It is probably dangerous to implant more than 15 gms. of sulfanilamide in the peritoneal cavity at any one time. Following implantation of sulfanilamide in the peritoneal cavity, the blood levels may rise quite high if large amounts are used; and the blood level in milligrams per cent may be expected to rise to approximately the same figure as the amount of the drug in grams which is implanted in the peritoneal cavity. Thus, if 10 gms. of the drug is implanted, a blood level of approximately 10 mg. per cent can be anticipated.

Question 2: As yet there is little evidence to indicate that the healing of clean wounds is seriously affected by the local implantation of reasonable amounts of sulfanilamide or its derivatives. If very large amounts are used, an increased serous discharge may be produced, but the prophylactic treatment of uninfected wounds requires only a light sprinkling of the powder and should not entail the implantation of large amounts. We have observed no apparent retardation in the epithelialization of clean burns following the local use of small amounts of sulfanilamide.

Question 3: Since sulfathiazole is much more effective against the staphylococcus than sulfanilamide, the local use of sulfathiazole may be preferable in the treatment of staphylococcic infections. However, as a matter of practical usage, the local concentrations of the drugs are so high that the cheaper sulfanilamide appears to be nearly as effective as the much more costly sulfathiazole. Accordingly, we prefer to use sulfanilamide locally in the prophylaxis and treatment of wound infections except in cases of stubborn staphylococcic infection. There is

never any indication for the simultaneous use of more than one of the sulfonamide drugs.

Question 4: We have not found it necessary to sterilize sulfanilamide powder before applying it to either clean or infected wounds. The powder, as it comes from the factory, is either so sterile that further sterilization is unnecessary, or its bacteriostatic powers in the tissues are so strong that any organisms are promptly destroyed. In any case, we have observed no infections in clean wounds into which sulfanilamide has been implanted, nor have we seen any reports of infections arising in clean wounds following its use.

WOUND INFECTIONS

In spite of the prophylactic, local and systemic use of the sulfonamide drugs in patients with contaminated surgical wounds, wound infections still are important and occasionally serious postoperative complications. Here again we cannot afford to rely upon chemotherapy alone, and adequate surgical drainage must be afforded in cases in which suppuration occurs. This fact was strikingly shown in a recent case of the most fulminating wound infection we have ever seen.

The patient had had a gastric resection for a very extensive carcinoma of the stomach. Twenty-four hours after the operation, the patient's temperature was 104° F. He was delirious and toxic, and examination of the wound showed a brown serous discharge and a fulminating cellulitis of the entire abdominal wall, with gangrene of the skin edges extending for an inch or more on each side of the incision. The induration, tenderness, and redness extended laterally on the left into the flank and back. Culture showed hemolytic streptococcus and colon bacillus. Sulfapyridine was given intravenously, and within twelve hours, the temperature had fallen abruptly, the patient was rational, and the spreading cellulitis was controlled. Suppuration, however, had taken place in the incision and the fascial spaces of the left flank. In spite of the local and systemic use of sulfanilamide and sulfapyridine, the incision continued to drain, the patient maintained a low grade temperature, and failed to regain his strength and appetite. Not until the subcutaneous tissues of the left flank were adequately drained by wide incision of the overlying skin did the infection finally clear up.

Before the advent of sulfanilamide, the infected area would have been treated by much earlier debridement and dependent drainage. The brilliant result from the treatment of the cellulitis made us too optimistic about clearing up the suppuration and resulted in considerable delay in the institution of adequate drainage. The limitations, as well as the assets of the sulfonamide drugs, must be recognized if such errors in judgment are to be avoided.

GEORGE CRILE JR.

CARBUNCLE

A carbuncle, in its early stages, is a cellulitis from infection with the staphylococcus. Later in its development, a carbuncle suppurates to form many small abscesses. During the early cellulitis stage, a carbuncle may be amenable to treatment with sulfathiazole. Later, however, when extensive suppuration has occurred, a carbuncle rarely responds dramatically to sulfathiazole. Chemotherapy alone can only limit the further extension of the cellulitis and prevent the development of septicemia. Adequate surgical drainage or excision is still indicated, but the operation is less radical than if sulfathiazole were not used.

Roentgen therapy in the early stages of the infection also has been of value in our experience. With roentgen therapy, immobilization of the part, and application of moist heat, surgery has been avoided in nearly 50 per cent of the carbuncles so treated. After incision or excision of a carbuncle, the wound should be packed with sulfanilamide.

PHAGYDENIC ULCERS

Phagydenic ulcers are necrotizing, burrowing, subcutaneous infections, as a rule caused by streptococci and staphylococci living in symbiosis, and may respond dramatically to sulfanilamide or sulfathiazole given by mouth. More frequently, however, they react favorably to the direct application of the drug in the wound, and rarely do they fail to respond to a combination of wide debridement of all undermined skin with immediate application of large amounts of sulfanilamide in the wound. The treatment of choice before the advent of the newer chemotherapy was the application of zinc peroxide, which is now less frequently required to control these infections.

The same principle governs the treatment of phagydenic ulcer as that of any abscess. As long as pus, exudate, or the products of proteolysis are present, the sulfonamide drugs will not effectively control the infection. Wide surgical debridement is essential to remove all pockets and foci for the accumulation of pus. When these foci are eradicated, the sulfanilamide can effectively deal with the infection.

The importance of debridement is illustrated by a recent case of a huge phagydenic ulcer of the lower leg which originated in an insect bite. Although sulfanilamide and sulfathiazole had been given orally in adequate doses, the ulcer had continued to enlarge until at the end of five weeks it was six inches in diameter. A culture taken on admission showed nonhemolytic streptococci and staphylocci.

Sulfathiazole powder was sprinkled upon the wound and was packed under the overhanging skin edges. In spite of the frequent local application of large doses of sulfathiazole and the use of moist heat, the ulcer

continued to spread and the patient ran a low grade temperature. The open area of the ulcer became very clean, but the infection continued to burrow beneath the edges with the accumulation of secretions. The infection was not controlled until the overhanging flaps of skin were cut away and the wound was again sprinkled with sulfanilamide powder. Within a week, the wound was so clean that split thickness grafts were applied with a 100 per cent take.

SYSTEMIC REACTION TO INFECTION

When infections are treated with chemotherapy, the temperature frequently falls promptly to normal, and the patient appears to be cured of his infection. Despite this dramatic clinical response, the infection may, by no means, be eradicated. Too often there are residual pockets and abscesses in which, because of the presence of pus and products of proteolysis, the infection persists. Under these circumstances, the systemic reaction of the patient at first may give no clue to the presence of these abscesses. Not until after the drug is discontinued, does the patient's temperature again rise with evidences of persistent infection.

The explanation of this phenomenon is not entirely clear, although the chemotherapy may control the infection in areas of cellulitis around the abscess pockets, and accordingly reduce the absorption from these points, which was well illustrated in the case of a woman who had a diffuse staphylococcic peritonitis. With large doses of sulfathiazole, her temperature fell to normal and remained so. Even the abdominal distension subsided, and it seemed that she would recover. After her temperature had been normal for several days, she became unconscious and died, still without any elevation of temperature. Postmortem examination of the abdomen showed multiple large and small abscesses scattered throughout the entire peritoneal cavity, all of which were filled with pus. Chemotherapy had masked the signs which such an infection normally produces.

Since the sulfonamide drugs can so completely mask the systemic symptoms of residual abscesses, it is important to be constantly on the alert if abscesses are to be detected and adequately treated by surgical drainage.

CONCLUSIONS

The advent of chemotherapy has not significantly altered the surgical attitude towards suppuration and abscess. Chemotherapy alone cannot take the place of adequate surgical drainage. However, since the development of chemotherapy, the surgical approach to acute infections need not be so radical as in the past. The use of sulfonamides in the treatment of acute surgical infections does not supplant surgery, but acts as a valuable supplement to sound surgical practice.

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THE TREATMENT OF FRACTURE OF THE PATELLA

JAMES A. DICKSON, M. D.

In the treatment of fracture of the patella, the most ideal procedure is that which will return the kneejoint to normal range of motion with the minimum of resultant traumatic arthritis. It is also very important that this procedure be accomplished with a minimum of time lost.

The consensus of opinion is that the vast majority of cases of fracture of the patella should be treated by open operation. The operative procedure generally adopted is thorough exploration of the fracture, removing all blood clots, replacing the fragments, and maintaining their position by means of a purse-string suture of silk or wire. This procedure is by no means simple. Even experienced and meticulous surgeons find it wrought with difficulties that often are not sufficiently emphasized. It is very difficult to prevent a certain tipping of one or more fragments, which results in roughness on the undersurface of the patella (Fig. 1 A and B). In the literature there are many suggestions for various methods of insertion of the sutures in an attempt to avoid this complication. The fact that there are so many methods only emphasizes the difficulties encountered. If this roughening occurs, it causes a grating or crepitation of the kneecap when motion is started, which is very annoying to most patients, and definitely prolongs the time of gaining full range of motion

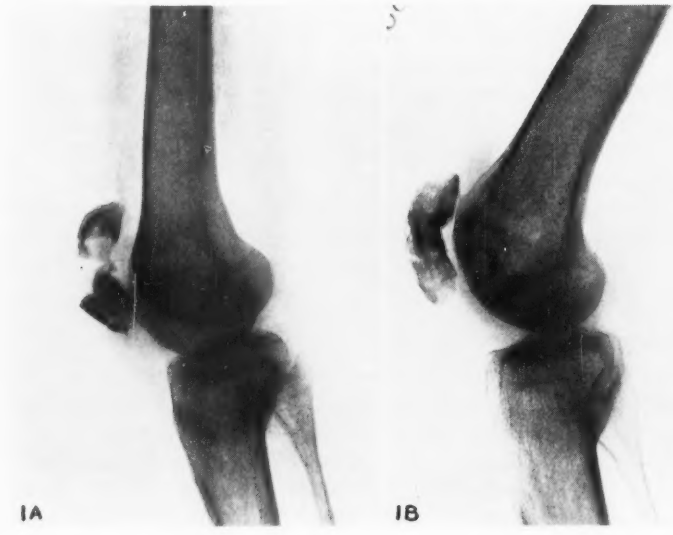

FIGURE 1: A. Fractured patella.
B. Showing roughness on the undersurface of the patella.

in the knee. In some instances where this irregularity is marked, it is often impossible to procure full flexion of the knee-joint even after months of treatment.

J. E. M. Thomson, in 1935[1], suggested the removal of the comminuted fragments or the smaller fragment. This procedure has proved most satisfactory in eliminating the irregularity of the under-surface of the patella. With certain modifications I have used this procedure for a number of years with such uniformly gratifying results that I feel justified in emphasizing the advantages of this operation in fractures of the patella.

The operative procedure which I prefer, is the exposure of the patella through a longitudinal incision over the front of the knee, extending from about four inches above the patella to the attachment of the patellar tendon, reflecting the flaps sufficiently laterally to expose the tears in the capsule of the joint. The patellar tendon is then split longitudinally (Fig. 2A) and all the comminuted fragments are removed. An incision is then made over the remaining portion of the patella and the perisoteal covering is reflected. A V-shaped strip of the quadriceps tendon is then freed, leaving the lower end attached and of

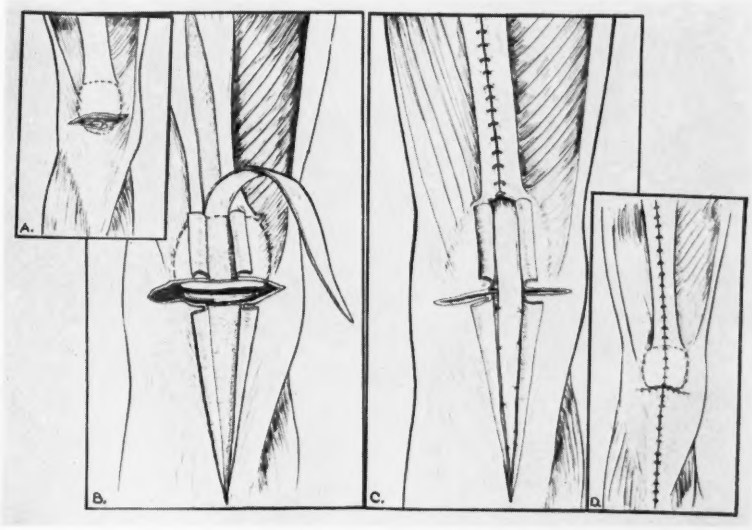

FIGURE 2: A. First incision over the front of the knee.

B. V-shaped strip of quadriceps tendon is freed, leaving the lower end attached.

C. and D. Edges of the quadriceps tendon are sutured into place and the lateral tears of the capsule repaired.

sufficient length to reach to the tibial tubercle (Fig. 2B). This strip of tendon is fixed firmly in place by sewing the reflected portions of the patellar tendon and periosteum on the anterior surface of the patella over the transplanted tendon. The edges of the quadriceps tendon are sutured into place and the lateral tears of the capsule repaired (Fig. 2 C and D). Chromic catgut is used throughout the repair. One point in the technic to be emphasized is that in placing the fascia strip in its new bed, care must be taken not to shorten the patellar tendon, for in so doing much time can be saved in regaining full range of motion in the joint. The transplanted piece of tendon aids greatly in filling the defect caused by removal of fragments and facilitates repair of the patellar tendon. The skin incision is then closed and the knee supported by means of a posterior plaster splint.

Quadriceps exercises are instituted in ten days and all protection is removed at the end of the third week. The range of motion gradually increases and by the end of six weeks a stable joint with 90 degrees of motion is obtained and the patient usually is able to return to his former occupation. Complete range of motion has been procured by time and use, until normal range of motion is established.

The advantages of this operation for the repair of a fractured patella is that the problem of bone repair is changed to one of liga-

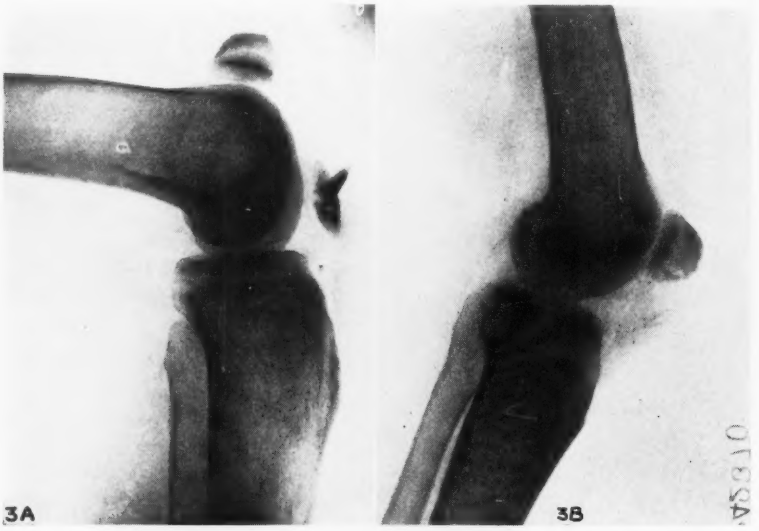

FIGURE 3: A. Showing fractured patella.
B. Degree of repair six weeks after operation. There is full range of normal motion and the patient was able to return to his regular occupation.

mentous repair. The quadriceps muscle is well anchored to its tibial attachment, so there is no danger in starting early motions of the knee. The degree of bony repair of the patella does not have to be determined before instituting motion. By this procedure the possibility of a rough undersurface with its complications is also eliminated. In our experience the time necessary for return to normal function has been greatly facilitated.

The results in two typical cases are presented in figures 3 and 4.

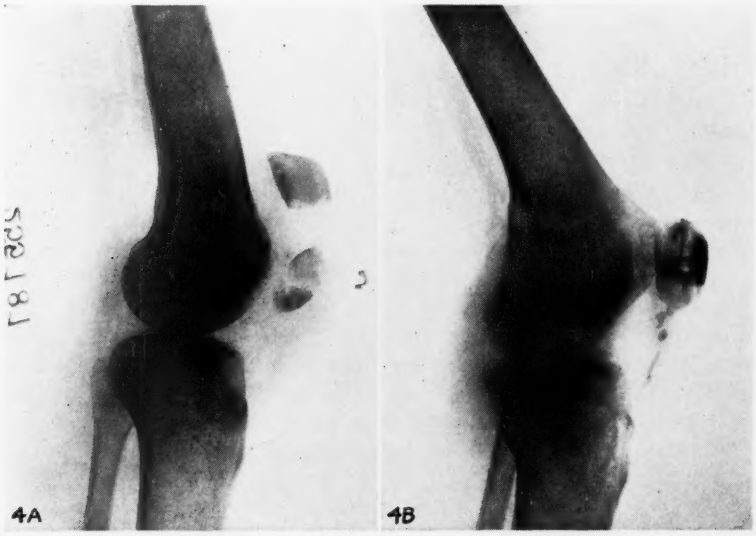

FIGURE 4: A. Showing fracture of patella.

B. Repair with some calcification in the patellar tendon; 90 degrees flexion in six weeks; full range of motion in twelve weeks.

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THE TREATMENT OF CHOREA WITH TYPHOID SHOCK

JOHN TUCKER, M.D.

Until recent years, it was doubtful whether any type of medical therapy had shortened the course of Sydenham's chorea. Standard medication consisted of prescriptions containing salicylates or some form of arsenic. Inasmuch as the disease usually subsided spontaneously in one to three months, medication probably influenced its course very little.

With the advent of nonspecific fever therapy, we now have a method of treatment which not only shortens the duration of the disease, but also prevents, to some extent, the onset of endocarditis and arthritis if it has not already appeared.

Many authors have advocated passive methods of raising the body temperature, such as the heat cabinet or the induction coil[1,2]. Like another group of investigators[3,4], we have employed intravenous typhoid and paratyphoid vaccine with the idea that active participation of the body cells in producing the rise of temperature resembles an active immunity, and that it is more likely to be effective at lower temperatures. We are listing in the order of importance some of the reasons for believing that our method of inducing hyperpyrexia by intravenous typhoid vaccine is especially worthwhile.

1. Safety — we have never had any serious reactions or complications in any case in which we have used this method of typhoid shock, regardless of the patient's age.

2. Comfort — patients do not complain of undue discomfort during the chill or secondary fever following the injection.

3. Control of fever — with the use of a modification of the method of Howard[5], we have not observed excessively high fever.

4. Economy — although the usual course of six febrile reactions requires a period of two weeks in the hospital, we have been able to discharge an occasional patient after two or three chills. At times, relief of symptoms has been marked after the first chill.

5. Convenience — although it is better to carry out treatment in the hospital, there is no good reason why the injections could not be given in the home under the direction of an intelligent mother.

The equipment needed is simple, and includes any standard preparation of typhoid and paratyphoid A and B vaccine, a 10 cc. luer syringe with needle, sterile normal saline in ampoules or freshly prepared, and a thermometer.

Our modification of Howard's method is as follows: The initial dose is 25 million for adults and 15 million for children under ten years. The bacteria are diluted in about 10 cc. of sterile physiological saline and given in the vein of the forearm. In one to three hours the patient has a chill followed by fever to 102.5 or 103° F. If a chill does not occur, the vaccine may have been administered extravenously unintentionally.

With the prompt rise of temperature, the patient has no feeling of depression, but rather the sensation of getting a slight "cold". Within two or three hours, the fever may drop rapidly or be followed by a secondary rise. As soon as the temperature remains fairly normal for 24 hours, the second dose of 50 million bacteria is given. Each subsequent dose is double the preceding dose until a total of six injections have been given. In other words the patient receives successively 25 million, 50 million, 100 million, 200 million, 400 million, and 800 million bacteria. We always allow an afebrile period of approximately 24 hours to elapse before giving the next dose.

Although we select our patients with some care, we find, as have others, that acute arthritis, myocarditis, or endocarditis do not increase the hazard of treatment. As a rule the swollen joints subside and pain is alleviated although this improvement is not always permanent. However, rarely is there a recurrence of the chorea after a full course of protein shock has been given.

We assume that the effect of nonspecific protein shock is twofold. First, the elevation of temperature in itself may have an unfavorable effect upon the causative agent, be it a virus or bacterium. Second, the cellular reaction of the tissues to the foreign protein may bring out several effects which contribute to the active defense of the body to the disease, such as increased capillary circulation, increased cellular oxidation, increased permeability of the cell membrane, increased exudation of serum from the capillaries, increased enzymes and antibodies, and leukocytosis accompanied by an increase in phagocytes.

It is reasonable to assume that such cellular and enzymic responses are more pronounced when the fever is produced by nonspecific shock methods than by the use of the heat cabinet, and yet there is no proof that such is the case. The favorable reports by Barnacle, Ewalt and Ebaugh[1] and by Kendell and Simpson[2] with the use of the Kittering hypertherm would lead us to believe that this is an effective method for the treatment of Sydenham's chorea. As fully as good results follow the use of intravenous typhoid vaccine, and as this method of therapy has been entirely safe in our hands as well as simple of operation, we believe that it can be employed by the average practitioner with the assurance that in the majority of instances he can bring prompt relief to his patient suffering with chorea.

A summary of the important points in 17 cases of chorea treated in the hospital is shown in Table 1. Most of the patients required the full course of six chills, although a few recovered after three to five reactions. In all but two patients, immediate recovery or decided improvement was noted while under hospital observation. One patient, a girl of 16 years, seemed to be worse during her treatments but recovered within a week after returning home and was well eight and a half months later. Her recovery occurred three weeks after the onset of the chorea and may have been a spontaneous cure.

TABLE 1

No.	Age	Sex	Rheum.	Tonsils Out	Duration Chorea	Grade	Previous Attacks	Heart Murmur	Immediate Results	Late Results
1	12	F	6 attacks	+	2 months	+	0	0	Recovered	Well, 4 months
2	16	F	1 attack	0	½ month	+++	0	0	Poor	Well, 8½ months
3	17	F	1 attack	+	1 month	+	0	+	Recovered	Well, 31 months
4	25	F	1 attack	+	2 years	++	9 attacks in 2 years	0	Improved	Well, 5 years
5	13	F	?	+	6 days	+++	0	0	Recovered	Well, 8½ years
6	15	F	0	+	7 years	++	++	0	Improved	No improvement 10 years in State Hospital
7	17	F	?	?	1½ months	++	0	0	Recovered	No report, 11 years
8	7	F	0	0	2 months	+	0	0	Recovered	No report
9	13	F	0	+	5 months	++	2	0	Recovered	Well, 10½ years
10	15	F	1 attack	+	3 weeks	+	0	0	Recovered	Well, 2 months
11	10	F	0	+	2 weeks	+++	0	0	Recovered	Well, 2 months
12	16	M	1 attack	0	3½ weeks	++	0	0	Recovered	Well, 5 weeks
13	17	M	?	0	1 week	+	0	0	Recovered	Well, 2⅓ years
14	11	M	0	+	1 month	++	0	+	Recovered	Well, 2⅙ years
15	11	M	0	+	6 weeks	++	1	+	Improved	Well, 3 years
16	12	M	0	+	1 month	+++	1	0	Recovered	Well, 1½ years
17	14	M	+	+	?	++	1	+	Recovered	No improvement

Another patient (Case 6) who improved markedly in the hospital became worse upon returning home, and the ten year follow-up revealed that she is in a hospital for the insane. Although the case history does not record a family history of chorea, it is likely that she had Huntington's rather than Sydenham's chorea. One patient had two or three subsequent attacks of chorea, but is now well (Case 4).

Tonsillectomy had been performed in 12, or 80 per cent, of the cases previous to the attack of chorea. Obviously this procedure was not effective as a prophylactic measure. Previous rheumatism was recorded in 7, or 41 per cent, and of these two had an endocardial murmur. The other two cases of endocarditis gave no rheumatic history.

The sedimentation rate was estimated in 11 cases, and was high in only 4 cases, two of which showed an endocardial murmur. There was

no anemia in any instance, a slight leukocytosis in only 3, and a fever in 3 with a maximum of 100.8° F. From this data one might assume that all of the cases were mild and that the results might have been different in severe chorea. The records show that the majority of patients were very active cases although none were disturbed by muscular jactitations during sleep. Likewise, good therapeutic results were just as prompt in the severe as in the milder cases.

COMMENT

Even though Sydenham's chorea is usually a self-limited disease, we believe that it is worthwhile to terminate the disease as rapidly as possible. While there is no assurance that typhoid shock therapy will prevent a recurrence or guard against a subsequent attack of rheumatic fever or endocarditis, yet in our short series this has been the case in 80 per cent. Furthermore, the gratitude of the parents of these children, as well as the comfort of the patient, are factors that justify the use of this harmless therapy. We advocate the method of Howard since it has been found to be safe in our treatment of many hundreds of patients with various diseases. It works well in both old and young and there are few contraindications for its use. In severe cardiovascular renal disease, severe diabetes or advanced arteriosclerosis, any type of nonspecific shock treatment probably should be avoided. In children, however, the reactions cause little discomfort.

CONCLUSIONS

In a series of 17 cases of chorea, 16 of which had Sydenham's chorea, the results were satisfactory both early and late in 80 per cent. Typhoid shock therapy for this disease is simple, safe and economical. The results are gratifying.

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SUPRAPUBIC PUNCTURE IN THE TREATMENT OF NEUROGENIC BLADDER

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The treatment of "cord bladder", a disturbance of bladder function from disease or trauma of the spinal cord, can be a difficult problem. Until the recent publications of Munro, there was little physiological basis for whatever treatment was instituted. With the advent of tidal drainage and recognition of the various types or stages of a given cord bladder, more satisfactory results have been obtained.

In his excellent work on the cystometry of the bladder Munro[1,2] classifies "cord bladders" into four groups:

1. Atonic — characterized by retention and extreme distention from lack of detrusor tone, lack of any activity of the external urethral sphincter, and complete lack of emptying contractions.

2. Autonomous — the detrusor and internal sphincter musculature show signs of reciprocal action of varying degree. There is an increase in detrusor muscle tone, and an inability to store an appreciable amount of urine without leakage. The condition of this bladder represents the end result in destructive lesions of the sacral segments or cauda equina.

3. Hypertonic — an expression of an uncontrolled spinal segmental reflex, characterized by a markedly increased detrusor muscle tone, almost constantly present emptying contractions, low residual urine, and impairment of control of the external sphincter.

4. Normal cord bladders — in transecting lesions above the sacral segments, consisting of two types which differ largely only in their cystometric findings:

(a) Uninhibited cord bladder — an apparently normal bladder which empties itself quite regularly. The detrusor tone is still somewhat increased, emptying contractions are rhythmical, the residual is low, and the capacity is rather low.

(b) Normal cord bladder — an apparently normal bladder with a return of subjective control. The tone of the detrusor muscle is only slightly increased, the capacity is greater, and a small amount of residual urine remains.

With the aid of the tidal drainage apparatus, and a knowledge of the various pressures applicable in promoting a more satisfactory recovery in the transitions of a given cord bladder through certain of the above stages, Munro reduced the incidence of bladder infection from

73 to 15 per cent. This is a remarkable advance in the treatment of a condition, in which infection was the chief cause of death. Since Munro's work deals essentially with observation and treatment of the acute spinal cord lesion, its applicability not only in the urological field but also in the neurosurgical becomes evident.

The relatively acute "cord bladder" in neurological cases, whether postoperative or caused by a rapidly progressing disease of the spinal cord, affords the most satisfactory application of this treatment.

It is felt that, as in other muscles affected by a lesion of the central nervous system, a certain progressive degenerative change in the involved portions of the genitourinary system occur[3], and that proper drainage will favor such repair as is anatomically possible. It is well known that suprapubic cystotomy will adequately drain such a bladder for years[4] with little regard for the possible maximum correction of a disturbed physiology, and with a very low incidence of infection. In the acute cord bladder the use of tidal drainage with the indwelling catheter, recommended by Munro, deals efficiently with the re-establishment of as normal a physiology as possible at once but possibly with the added risk of infection from its presence. The long-continued use of the indwelling catheter in even a very mildly septic prostate, bladder, or

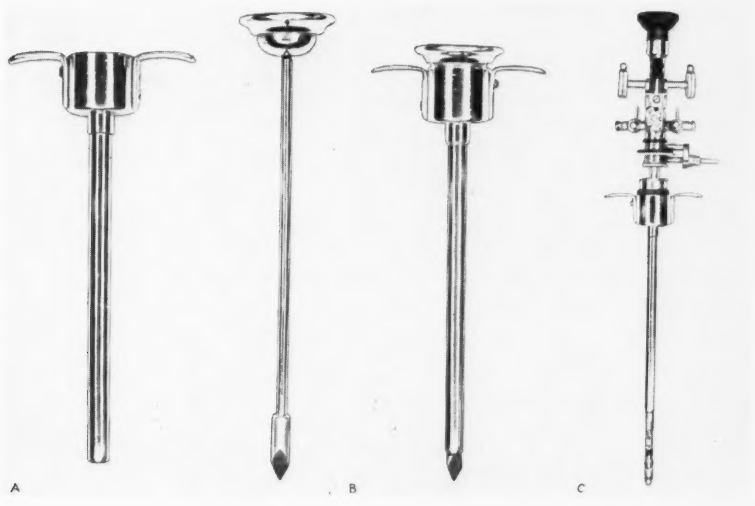

FIGURE 1: A. Cannula and trocar.

B. Instrument assembled.

C. The McCarthy Cystoscope is inserted into the cannula for visualization of the bladder.

urethra undergoing acute changes from disruption of nerve supply always will constitute a menace in a certain number of these cases. It seems that the problem is that of gaining efficient drainage of the bladder with the minimal risk of infection and still encouraging the resumption of as normal a physiology as the lesion of the central nervous sys-

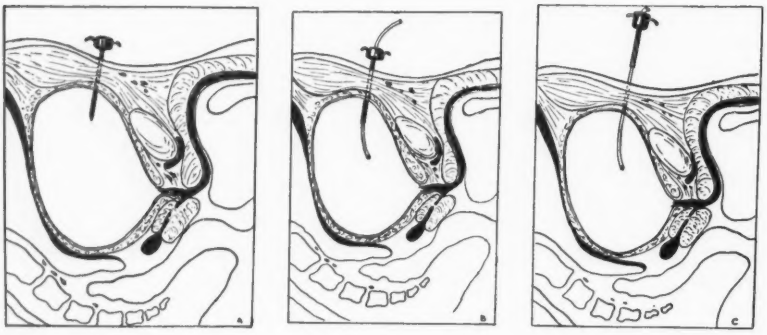

FIGURE 2: A. The trocar and cannula have been plunged into the bladder.

B. The trocar has been removed, and a No. 18 catheter inserted through the cannula into the bladder.

C. The cannula has been withdrawn, leaving the catheter in situ for suprapubic drainage.

tem permits. When this is accomplished, either natural or artificial drainage must continue to prevent pressure changes from occurring in the genitourinary system.

After experience with the indwelling catheter in the tidal drainage management of acute cord bladders at the Cleveland Clinic, it was decided that the use of the suprapubic catheter was worthy of a trial. This has been done in a series of cases with gratifying results from the standpoint of the patient, the surgeon, and those responsible for the nursing care.

CASE REPORTS

Case 1: A white man, 51 years of age, was admitted by ambulance after a rapidly progressive paraplegia developed following a lumbar puncture and lipiodol study. The neurological signs indicated an extramedullary cord tumor at the ninth dorsal vertebra. Complete urinary retention had been present since the lumbar puncture on the previous day, as well as marked urosepsis.

Operation: Under pentothal anesthesia a thoracic laminectomy was done and an extramedullary tumor (meningioma) was removed at the level of the ninth dorsal vertebra. The spinal cord was very edematous at the site of the tumor.

Progress: On the first postoperative day suprapubic puncture was decided upon because of the complete urinary retention. Under local anesthesia a small transverse incision was made above the symphysis and a trocar and cannula plunged into the bladder. A No. 18 catheter was inserted through the trocar and the trocar removed

after the catheter was fastened in place on the abdomen. The Munro tidal drainage apparatus was attached to the catheter.

Steady improvement in the patient's general condition then followed. There was marked improvement in the neurologic picture, and in three weeks the patient's bladder had changed from an atonic to an autonomous cord bladder. He was discharged after one month, still using the suprapubic tube to irrigate the bladder. The infection had subsided within a few days after instituting this regimen.

Case 2: A 46 year old white man was admitted with a complaint of rapidly progressive paresthesia and motor weakness from the chest downward. A small tumor of the chest wall had been removed one year previously. Pain in the back was a prominent feature of his illness for two months prior to admission. Two days before admission to the hospital an acute urinary retention developed suddenly, necessitating catheterization. The temperature from the cystitis was 102.4° F. on admission.

The neurologic signs indicated an extramedullary metastatic cord tumor at the level of the second or third dorsal vertebra. Lumbar puncture revealed a total block with a spinal fluid protein of 330 mg. Roentgenograms revealed a partial collapse of the third dorsal vertebra due to tumor.

Operation: Under avertin anesthesia a laminectomy was done from the sixth cervical to the fourth dorsal vertebrae and a soft vascular tumor was found extending the length of the exposure in the extradural space. A large portion of the tumor was removed and a decompression provided. The tumor was diagnosed as a sarcoma. Upon completion of the laminectomy a suprapubic puncture was done. The skin was prepared and infiltrated with 5 cc. of novocaine above the symphysis pubis. After nicking the skin, a trocar and cannula was plunged into the bladder. A No. 18 catheter was inserted through the trocar and the trocar removed. The catheter was fastened to the abdominal wall and the tidal drainage apparatus connected to the catheter.

Progress: The cystitis subsided moderately under treatment but an elevated temperature caused some concern. The laminectomy wound broke down on the twentieth postoperative day and discharged necrotic, purulent tissue. The wound was curretted and packed open. This improved gradually until at the time of discharge, two months after admission, the laminectomy wound had only a small sinus leading into it. The bladder had gone from an atonic to an autonomous cord bladder. Its further improvement to one of the anticipated "normal cord bladder" types was probably hindered by the urosepsis. Irrigation was continued at home after his discharge. He returned five months later for roentgen therapy to the affected regions. No further improvement was noted, the suprapubic tube still was in place, but there was no evidence of urinary tract infection.

The use of the suprapubic puncture in these two cases of acute cord bladder complicated by urosepsis, together with the use of the tidal drainage, presented a very satisfactory method of managing a difficult situation. Physiological conditions were maintained by the tidal drainage to regain as much as possible of the normal function of the bladder, while the suprapubic puncture afforded a clean and convenient method of drainage in the presence of infection. With this method of treatment bladder infection has been reduced to a minimum by avoiding the prolonged use of a urethral catheter. In like manner renal infection has not occurred in cases in which suprapubic puncture and the Munro tidal drainage apparatus has been employed.

CONCLUSION

The use of a suprapubic catheter to drain the bladder in conditions associated with disease or trauma of the spinal cord is followed by

fewer complications in the urinary tract than when prolonged urethral retention catheter drainage is used.

The Munro tidal drainage apparatus can be attached to the suprapubic catheter in the same manner as when a urethral catheter is employed.

The introduction of the catheter through the trocar can easily be accomplished under local anesthesia and obviates the necessity of a more extensive surgical procedure to expose the bladder and institute drainage.

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AURICULAR PAROXYSMAL TACHYCARDIA IN AN INFANT

Report of a Case

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Important disturbances of cardiac rhythm are uncommon in infancy, but one which occurs occasionally is auricular paroxysmal tachycardia. The attacks of tachycardia usually develop suddenly and are characterized by a regular rhythm at an extremely rapid rate. The paroxysms generally last for a few minutes to several hours, and the reestablishment of normal rhythm is, as a rule, abrupt. Many attacks terminate spontaneously or as the result of vomiting, while others can be brought to an end by pressure on the carotid sinus. It is only rarely that drug therapy is necessary. The present case is reported because of the long duration of the attack, its systemic effect on the patient, and the difficulties encountered in restoring normal rhythm.

CASE REPORT

The patient, a white boy 12 months of age, was admitted to the hospital on August 11, 1940 because of refusal to eat, diarrhea, loss of weight and tachycardia. Diarrhea, refusal to eat and occasional vomiting had developed about five weeks earlier, and after these symptoms had been present for ten days or two weeks, it was noted that the heart rate was extremely rapid. The tachycardia had persisted until the present without interruption. The infant refused practically all of his feedings and whenever he did take even a small amount, a considerable part of this was promptly regurgitated. The diarrhea, however, had improved gradually although at the time of admission there were still two to five movements each day. The body weight had decreased from 25 pounds at the time of onset of the symptoms to 18 pounds at the time of entering the hospital.

The past history was irrelevant except for a short attack of probable auricular paroxysmal tachycardia coincident with a gastrointestinal disturbance at the age of 3 months.

The general physical examination revealed a poorly nourished, dehydrated, restless infant. The temperature was 99° F and the pulse rate, 200 per minute. There was no engorgement of the peripheral veins. Pressure on the carotid sinus in either side of the neck had no effect upon the heart rate. The lungs were clear on percussion and auscultation. The heart was not enlarged; its rhythm was regular, and no murmurs were heard. The liver was not enlarged or tender, and there was no peripheral edema.

The urine had a specific gravity of 1.028 and contained a faint trace of albumin but no sugar or abnormal cellular elements. The red blood cell count was 5,590,000 per cu.mm. and the hemoglobin content 68 per cent. The leukocyte count was 6,800 per cu.mm. The Wassermann reaction of the blood was negative. Roentgenologic examination of the chest showed the heart to be within the limits of normal in size, shape and position. The electrocardiogram revealed auricular paroxysmal tachycardia with a rate of 230 per minute (Fig. 1).

During the first 48 hours in the hospital, treatment consisted only of the administration of liberal amounts of physiologic solution of sodium chloride containing 3 per cent glucose. The tachycardia persisted and the symptoms remained unchanged. On the third day in the hospital, mecholyl, 5 mg., was given by subcutaneous injection. Within a few seconds the heart rhythm became irregular and the rate dropped to approximately 70 beats per minute. The reduced rate, however, per-

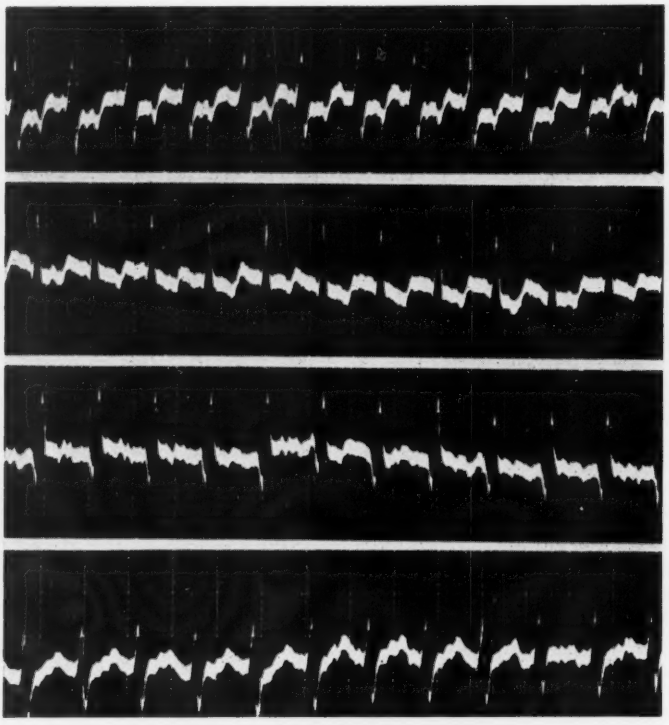

Figure 1: Auricular paroxysmal tachycardia. The rhythm is perfectly regular and the rate 230 per minute. The P waves distort the S-T segments and are diphasic or inverted in Lead 1, inverted in Lead 2, upright or diphasic in Lead 3, and upright in Lead 4F. The P-R interval is approximately 0.14 seconds.

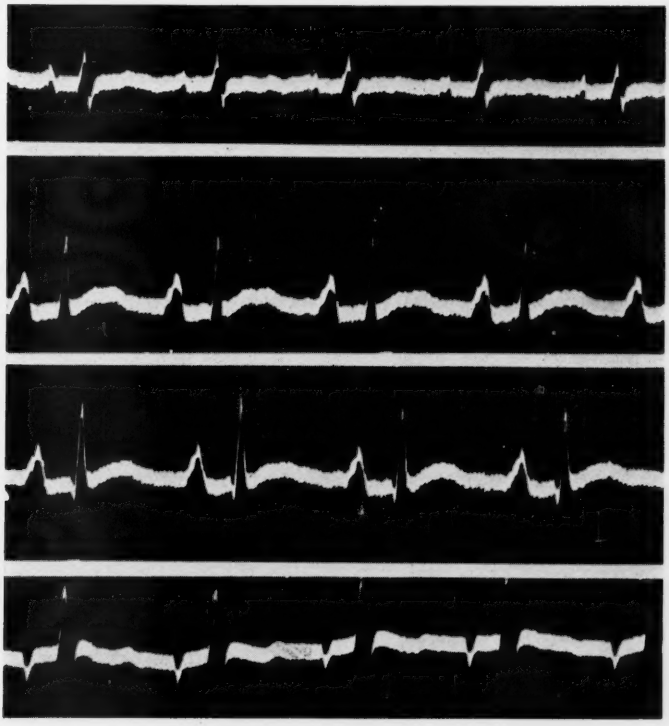

FIGURE 2: Normal rhythm. The rate is 100 per minute. The P waves are prominent and notched in Leads 2 and 3 and the P-R interval approximately 0.18 seconds. The T waves are flat in Leads 1 and 4F and are somewhat distorted by U waves in all leads. A tendency toward right axis deviation is present. The patient had received 2.75 cat units of digitalis.

sisted for not more than two minutes, and the tachycardia then returned. One and one-half hours later a second dose of mecholyl of the same size was administered, but this time neither the rhythm nor the rate of the heart was affected. On the following day, 7.5 mg. of mecholyl were given, and again the heart rate decreased to approximately 70 beats per minute and the rhythm became irregular. The tachycardia, with a rate of 240 per minute, returned within slightly more than one minute. Fifteen minutes later a second injection of the same size had the same transient effect. Several hours later quinine dihydrochloride, 60 mg., was administered by intravenous injection but without effect on the heart rate or rhythm.

On the morning of August 15 the administration of a digitalis preparation suitable for parenteral use and containing one cat unit

of digitalis bodies in 2 cc. of solution was begun by intramuscular injection. The first dose was 1 cc., and two additional doses of 0.5 cc. were given at intervals of six hours. The heart rate remained unchanged, and on each of the next two days the patient received three doses of 0.5 cc. each. During the night after the last of these injections the heart rate was noted to have dropped to 106 per minute. At eight o'clock the next morning, however, the rate was 136 per minute and two hours later it had increased to 168. One-half cubic centimeter of the digitalis preparation was given, and within the following two hours the rate dropped to 120 beats per minute. A further decrease in rate to 100 per minute occurred in the next twelve hours (Fig. 2) and the rate was maintained at approximately this level during the remainder of the stay in the hospital. No further medication was given, and the patient was discharged on August 22.

With the control of the tachycardia, the general symptoms began to improve quite promptly. The patient began to take his feedings regularly and vomited but once during the rest of the time in the hospital. The diarrhea also lessened although some looseness of the bowels remained for several days after discharge from the hospital.

A letter from the referring physician six months later states that about one week after the patient returned home there was a paroxysm of tachycardia with a rate of 200 per minute which came on during a prolonged crying spell and lasted but a few minutes. Except for this the child had been perfectly well and now weighed 31½ pounds.

SUMMARY

A case of auricular paroxysmal tachycardia in an infant 12 months of age has been reported. The paroxysm apparently developed as a complication of a gastrointestinal disturbance and in turn seemed to be responsible for the persistence of refusal to eat, regurgitation of the small amount of food taken and diarrhea. Although there was no detectable evidence of congestive heart failure, it is probable that the continuation of symptoms was due to passive congestion in the liver and gastrointestinal tract. The tachycardia continued without interruption for a little over four weeks, and the heart rate during this time ranged from 200 to 240 beats per minute.

Pressure on the carotid sinus in either side of the neck had no effect upon the heart rate. Mecholyl was administered by subcutaneous injection on four occasions. Three of the injections resulted in a prompt

decrease in the heart rate to approximately 70 beats per minute, and the cardiac rhythm at the same time became irregular. These effects were of transient nature, however, and the tachycardia was resumed within two minutes' time. The intravenous injection of quinine dihydrochloride on one occasion did not influence the heart rate or rhythm. The intramuscular administration of a digitalis preparation resulted in the restoration of normal rhythm after a total of 2.5 cat units of digitalis bodies had been given in divided doses in a period of 60 hours. The heart rate increased to 168 per minute within the following few hours, but after an additional 0.25 cat units of the digitalis preparation, normal rhythm was reestablished. With the control of the tachycardia the general symptoms promptly began to improve.

UMBILICAL CONCRETIONS

W. J. ENGEL, M.D.

Although lesions of the umbilicus are not common, they have received scant attention in the literature. Two cases recently came under my observation within a few weeks of each other and were of sufficient interest to report briefly. In each case an umbilical concretion was responsible for the patient's symptoms, and prompt and complete relief was afforded by simple removal of the foreign substance.

CASE REPORTS

Case 1: A 24 year old student came into the Clinic in December, 1940, to consult the dermatologist. He complained of soreness and tenderness of the umbilicus, which had been present for several days and was becoming worse. More recently he had noted some discharge from the umbilicus. He had never had any previous symptoms and his general health had always been good. The history of the systems was without significance.

The general physical examination was essentially normal. A thin watery discharge was observed exuding from the umbilicus, which was rather deep with considerable redness and edema at the bottom. Manipulation attendant to examination was quite painful. There was some tenderness surrounding the umbilicus. The original impression of the examiner was patent urachus, and the area was painted with gentian violet.

One week later the patient stated that he was much better, and the same treatment was applied. He returned in another week, however, and complained of greater discomfort and more discharge. A culture for yeast was taken, which was later reported negative, and 100 r of roentgen therapy was given.

Examination at the time of a subsequent treatment two days later revealed a small papillomatous lesion with superficial erosion upon the surface, located deep in the umbilicus. I was consulted at this time, and observed that in addition to the papillomatous lesion there was considerable redness, edema, and pronounced tenderness which partially interfered with adequate examination. Examination under anesthesia was advised to permit more complete inspection and also for biopsy.

The patient entered the hospital and was given intravenous sodium pentothal anesthesia. Upon separating the umbilicus with a small ear speculum, some dark gray material was observed very deep in the umbilicus beyond a very small fibrotic opening. After dilating this fibrotic ring, a mass of hair and gritty material held together by sebaceous material was removed piecemeal. The entire concretion was about the size of a large olive seed and when removed, left a deep cavity extending downward. Following the removal of the concretion, a small piece of the papillomatous lesion was taken for biopsy, a section of which showed only a well-marked inflammatory reaction, but no evidence of neoplasm.

The patient had an uneventful convalescence; the lesion healed completely; and he has remained well since that time.

Case 2: A housewife, 44 years of age, came into the Clinic for examination for "heart trouble", and the lesion to be reported here was incidental to her chief complaint.

For three years she had observed recurrent attacks of itching about the umbilicus, followed by the formation of a small "blister" which would rupture and drain. Occasionally she had been able to express a small amount of pus from the depth of the umbilicus, which was associated with some tenderness. The last attack had occurred about one week previously, and a small amount of discharge was still present. A patent urachus was suspected, and she was referred for further study.

Examination revealed a deep, narrow umbilicus from which a small amount of thin, ill-smelling, seropurulent discharge exuded. Some redness and deep tenderness was observed and on carefully separating the walls of the umbilicus with narrow retractors, a small grayish concretion the size of a large grape seed was brought into view. The concretion consisted chiefly of sebaceous material and gritty foreign particles with epithelial cells. Complete removal relieved the patient from further symptoms from this source.

DISCUSSION

Concretions may be considered one of the more common lesions of the umbilicus. They probably occur only in the deep, narrow type of umbilicus, and this anatomical fault is thus a predisposing factor. A foreign body such as cotton or wool fibers, hair, powder, dust, etc. settles in the deeper portion and sets up an irritation. Nature responds by secreting sebaceous material and forming epithelial cells which are cast off and increase the mass. Later, inflammatory changes may produce a stensosis of the opening, and imprison the concretion which gradually increases in size because it cannot possibly be extruded through the opening. Finally, the extensive irritation leads to severe inflammatory changes, and the patient seeks relief. This lesion does not imply uncleanliness, as it may occur in very meticulous individuals.

The concretions vary greatly in size from that of a pea to a pigeon's egg. They usually contain hair and cloth fibers, as well as gritty, sandy particles bound together with caseous, sebaceous material containing desquamated epithelial cells. Other foreign bodies such as stone fragments, beads, etc. may settle in the umbilicus and serve as the nucleus of a concretion.

The two most common presenting symptoms are pain and discharge from the umbilicus. According to the intensity of the inflammatory process, the pain varies from mild pain and tenderness, to severe pain, swelling and fever associated with abscess formation. The periodic discharge of a thin serous or seropurulent secretion should always lead one to suspect this lesion.

Examination may be relatively insignificant, and the true nature of the condition be overlooked. Concretions may lie very deep, and the opening may be so small as to prevent visualization of the concretion. The swelling may be slight and cases have been reported in which the swelling was some distance from the umbilical depression. Some discharge which is usually malodorous is almost invariably present.

Several factors may be considered in the differential diagnosis. As in our first case, tumor was suspected, and these cases have been mistaken for cancer. They may simulate any inflammatory lesion such as tuberculosis or syphilis, both of which are exceedingly rare. Because of the presence of caseous material, some early cases are misdiagnosed as tuberculosis. Also, those containing quantities of hair have been errone-

ously reported as dermoids. Adequate exposure and inspection of the umbilicus, under anesthesia if necessary, is essential, and the presence of a quantity of sebaceous material clinches the diagnosis.

The treatment consists in dilating the opening and thoroughly removing the concretion. Surgical excision of the sac is not necessary. Recurrence, although possible, is not often observed and probably the associated inflammatory reaction obliterates the cavity. Moreover, the patient who has had one concretion is thereafter very vigilant and careful about umbilical cleanliness, which undoubtedly is a large factor in the rarity of recurrence.

CONCLUSIONS

Two illustrative cases have been briefly presented which have described umbilical concretions as a cause of pain, tenderness, and discharge from the umbilicus.

The diagnosis depends upon careful exposure of the umbilicus and inspection of the deepest recesses of the umbilical depression, which in certain instances may require anesthesia because of the pain and tenderness attendant to the examination.

Treatment consists of simple removal of the concretion which was promptly followed by complete cure in both the cases here reported.

THE VALUE OF ASPIRATION LUNG BIOPSY IN DIAGNOSIS

With Illustrative Cases

H. S. VAN ORDSTRAND, M.D. and T. H. LAMBERT, M.D.

Aspiration lung biopsy is a very helpful adjunct in the diagnostic armamentarium of pulmonary disease. It is indicated in roentgenographically visible lesions of the bronchi, parenchyma, and pleura when all other studies (i. e., thorough sputum examinations, bronchoscopy, and bronchography) fail to be of diagnostic aid. With few exceptions, its chief indications follow a negative bronchoscopic examination in cases with nontuberculous lesions, regardless of whether they are of infectious or of neoplastic origin. When indicated, the value of the procedure has proved to well exceed its risk, and when performed with care, it is relatively inocuous.

Some authorities have regarded aspiration lung biopsy as a needless procedure in a peripheral lung tumor when no apparent contraindications to exploratory thoracotomy existed. They reason that the diagnosis as well as further operability of a lesion may be established only on surgical exploration. Our experience has shown that needless exploratory lung surgery has been prevented in certain cases by the use of aspiration needle biopsy, as will be shown in subsequent case reports.

Although aspiration lung biopsy has been performed for more than fifty years, it has been in use with relative frequency only in the past decade. The first diagnostic puncture of the lung was reported by Leyden[1] in 1883. The method was used for the purpose of obtaining organisms from a pneumonic lung. Other early observers mentioned the diagnosis of thoracic cavity tumors by probatory puncture. From 1889 to 1919 fatalities were reported from perforation of intercostal arteries and arteriosclerotic vessels in the lung parenchyma. These were elderly patients in whom rather large trocars were used for thoracenteses. Death was caused by hemorrhage into the pleural cavity, into the lung, and into the bronchi and trachea.

Sixty-five malignant neoplasms proved by needle puncture and aspiration were reported by Martin and Ellis[2] in 1930. These men were credited with popularizing "aspiration biopsy" and establishing it in the field of neoplastic diseases. In 1936 Sappington and Favorite[3] concluded that lung puncture by a needle was a reasonably safe and useful diagnostic procedure. They reviewed more than 2,000 cases of various investigators. Christie,[4] in 1937, mentioned the value of the examination of cells found in pleural fluid obtained by needle biopsy in a case of pleurisy with effusion complicating the picture of carcinoma of the lung.

Wrenn and Ferder[5], in describing a new instrument for aspiration biopsy, emphasized the importance of this diagnostic procedure in patients who balk at a cutting diagnostic biopsy. Craver and Binkley[6] reported 92 cases of suspected primary cancer of the lung in which aspiration biopsies were performed and concluded that the procedure in selected tumors of the lung was a valuable and relatively safe method of diagnosis, and that bronchoscopy will fail as a diagnostic procedure in a substantial percentage of cases of early primary cancer.

Before aspiration biopsy should be considered a means of diagnosis, a thorough history and physical examination should be done, and all systems should be checked carefully for distant primary tumor, although roentgenograms give evidence of a single lesion in the lung. Repeated sputum examinations should be made. If these reports are of no value in establishing a diagnosis, biopsy then may be considered if bronchoscopy is negative, or is not advisable, or is unfavorable.

Tumors may lie below the surface, and an incision through normal tissue might be necessary to obtain a specimen. Aspiration biopsy here may be a time-saving method for securing tissue for histological examination without surgical incision. The danger of dissemination of tissue or fungation of tumor tissue through the operative incision has been theorized by some observers and the surgical risk of obtaining specimens from deep-seated masses sometimes contraindicate surgical biopsy. These are indications for aspiration biopsy.

The incidence of pneumothorax after lung puncture is infrequent, and sudden death is quite rare, the latter in most cases being due to air embolism. If the needle is firmly attached to a syringe, this danger is not very great. Empyema after lung puncture is not increased in our experience. Formerly the procedure was not performed when evidence of a free pleural space was found. Transient hemorrhage has been mentioned by a number of authors. A knowledge of anatomy and physical diagnosis will exclude such accidents as puncture of the heart and large vessels, or an aneurysm.

Sufficient time should be spent in localizing and identifying the exact position of the lesion in the lung field before attempting an aspiration biopsy. Some physicians use roentgenograms placed against the patient's chest while in the sitting position, bony landmarks being correlated with roentgenograms. Identifying marks may be mapped out on the skin and the site of insertion of the aspiration needle marked and visualized firmly in case preparation of the field causes fading of the skin markings.

About one hour before the procedure is begun, the patients are given sufficient sedation to keep them quiet and to allay their apprehension. Mapping out the tumor under fluoroscopic control with the use

of a boundary of gentian violet painted on the skin prior to the lung biopsy often is helpful. The patient is placed in the sitting position, if possible, and the field is prepared with iodine and alcohol. Prior to the procedure the patient is informed that he may have more cough and may expectorate some blood after the procedure. At the site marked for insertion of the aspirating needle the skin is infiltrated with one per cent novocaine, and the subcutaneous tissues anesthetized in like manner.

The needle and syringe which we use are shown in figure 1. With firm pressure on the stylette, the long 15 gauge needle is inserted into the lung just above a rib margin, care being taken to estimate roughly the thickness and consistency of the pleura while the needle is being inserted. Entrance into the tumor mass can be detected usually by the increased resistance encountered by the needle as compared with the resistance of normal lung tissue. The stylette is withdrawn and the syringe is securely attached to the needle. Suction is created within the syringe by withdrawing the plunger several centimeters and screwing the handle down in position, thus allowing the pressure to remain constant without further manipulation of the plunger. The needle now is withdrawn approximately 2 cm. and is quickly inserted further into the tumor at a different angle with a quick turn to the right, cutting off part of the tumor tissue with the end of the needle, the vacuum retaining the specimen. The needle then is withdrawn from the chest wall, and the suction created in the syringe causes loosened particles of the tumor

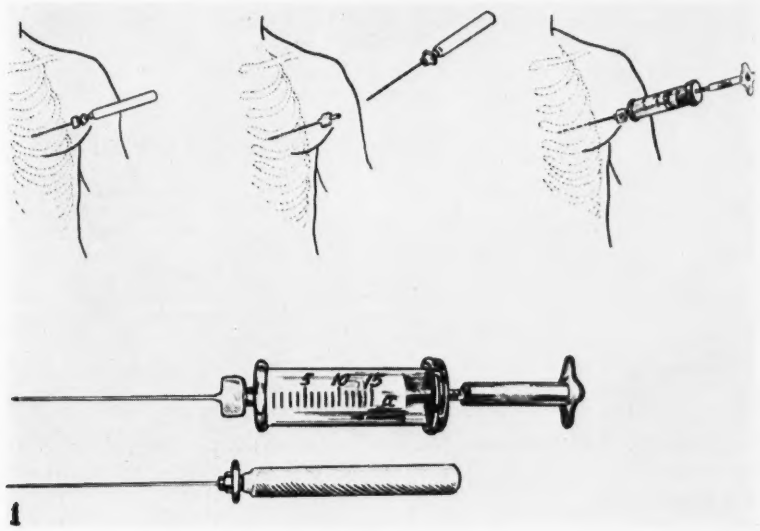

FIGURE 1: Instrument for aspiration biopsy.

tissue to be aspirated into the syringe. If blood enters the syringe during the aspiration, or if the patient starts to cough, the needle should be withdrawn immediately.

The aspirated material is sent to the pathological laboratory and a part to the bacteriological department (when indicated) where the precipitate is sectioned for microscopic study. It is fixed in formaldehyde and is then centrifuged. If the amount of aspirated material is small, it is centrifuged and the precipitate fixed with absolute alcohol for sectioning and study.

Aspiration biopsy has been used to a distinct advantage in establishing a diagnosis of pulmonary lesions in certain cases at the Cleveland Clinic when all other methods had been of no value.

The following cases of pulmonary lesions have been selected for presentation because of certain interesting features. They are of clinical interest because the impression prior to the biopsy procedure in most instances was at wide variance with the microscopic findings.

Case 1: R. H. S., a 49 year old man, was seen on February 5, 1940, complaining of low-grade fever and tachycardia of two months' duration. There had been a dull pain anteriorly in the upper left chest for one month. He had lost 12 pounds in weight during the two months' time.

A presumptive diagnosis of aneurysm had been made elsewhere. The entrance films are shown in figure 2A in which a mass is delineated in the upper left lung adjacent to the mediastinum.

The general physical examination was not contributory other than the presence of a dullness anteriorly between the levels of the first and third ribs on the left side, with an occasional moderate to coarse crepitent râle in this area. There were no objective signs of cardiovascular disease. The temperature was 99.2° F.

Bronchoscopic examination revealed considerable fixation of the trachea in the region of the mass, but no evidence of tracheobronchial ulceration. Fluoroscopy revealed no pulsation of the mass.

Under fluoroscopic control an aspiration needle biopsy was obtained. There was microscopic evidence of carcinoma (Fig. 2B).

Although the lesion was felt to be clinically inoperable, exploratory thoracotomy was performed at the insistance of the family. The tumor mass was found to involve the upper lobe of the left lung, and to extend well out into the superior mediastinum. The mass was quite firm and about the size of an orange. It was immobile and firmly attached to all surrounding tissues so that excision was impossible. The final diagnosis was bronchogenic carcinoma of the medullary type. The tumor cells were of fairly uniform structure with no tendency to form glands or pearls. Mitotic figures were numerous and in some areas the tumor cells were columnar in type and apparently secreted mucus.

The postoperative convalescence was uneventful. A course of roentgen therapy was administered to the lung tumor. Two subsequent courses were given in the ensuing ten months. The patient died of his disease one year after first being seen here.

Comments: This case was interesting in that a previous diagnosis of aneurysm had been made, this diagnosis being corrected by the aspiration lung biopsy.

Case 2: A. P., a 55 year old man, was first seen on January 27, 1940, with the chief complaint of soreness in the right chest. There had been a gradual development of

tenderness in the right upper chest for a year, and a tight feeling substernally. He developed a chronic cough which became more pronounced two weeks prior to his visit here. The sputum was blood-tinged. He had lost 15 pounds of weight in a year. A previous impression of his illness had been tuberculosis.

Physical examination revealed decreased expansion of the right lung, diminished tactile and vocal fremitus in the right upper chest from the apex down to the level of the seventh interspace anteriorly and the seventh thoracic vertebra posteriorly, with dullness to percussion over this area. There was a definite expiratory rhonchus over the entire right chest and numerous coarse and crepitant râles were heard in the right lateral upper lung field.

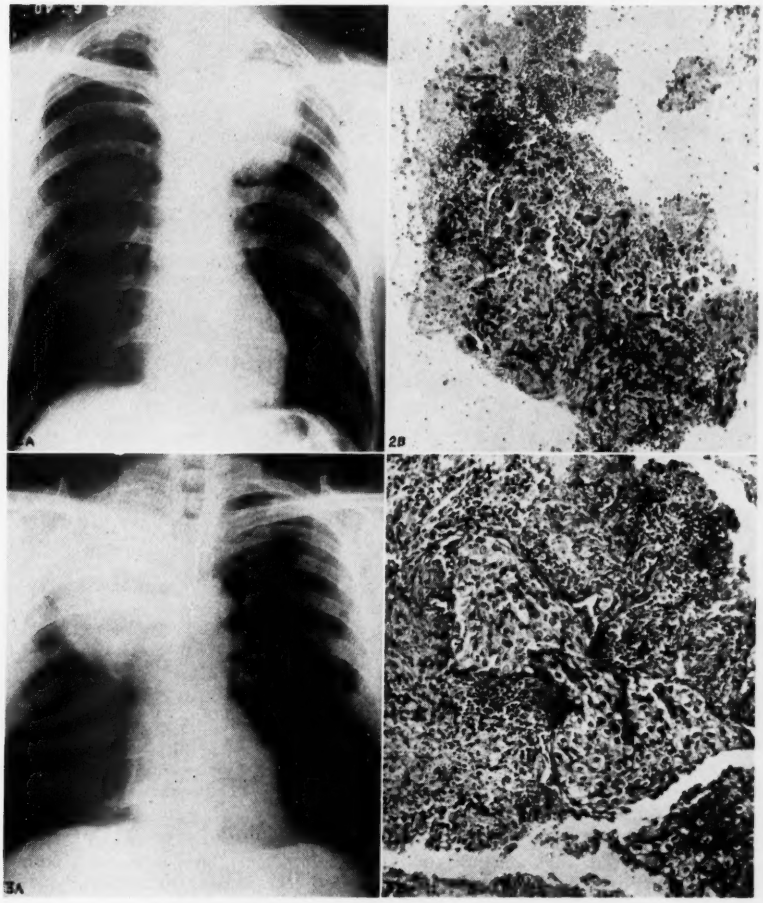

FIGURE 2: A. Bronchogenic carcinoma, upper left lung.
B. Photomicrograph showing medullary type of bronchogenic carcinoma.

FIGURE 3: A. Bronchogenic carcinoma, upper right lung.
B. Aspiration biopsy of lesion.

Roentgen examination of the chest showed a marked mottled density in the right upper lung extending down to the level of the lower border of the third anterior rib (Fig. 3A).

Bronchoscopic examination revealed the tracheobronchial tree to be entirely clear as far as could be determined.

In the aspiration needle biopsy the needle was inserted in the right first interspace, one and one-half inches from the sternal border. The microscopic examination of the sections showed fragments of tissue which appeared to be a bronchial mucosal type without tumor, along with numerous small and fairly large fragments of tumor tissue consisting of masses of large epithelial cells not forming glands or pearls (Fig. 3B).

On February 24, 1940 a right pneumonectomy was done. The patient died of empyema on the fourth postoperative day. The diagnosis was bronchogenic carcinoma.

Comment: In this patient a tentative diagnosis of tuberculosis was found to be incorrect on aspiration biopsy, carcinoma being found.

Case 3: G. R. O., a 75 year old man, presented himself for examination on November 22, 1940 with symptoms of a chronic productive cough, weakness, and night sweats of three months' duration.

The general physical examination revealed a temperature of 100.4°F. with positive findings in the right lung which consisted of a decreased note posteriorly from the levels of the second to the fifth thoracic vertebrae.

Roentgen examination of the chest revealed a well circumscribed ovoid shadow in the upper right lung (Fig. 4A, right lateral view). This was interpreted as probably being due to an interlobar empyema.

A bronchoscopic examination was negative.

Aspiration lung biopsy revealed the presence of tumor cells. No fluid was obtained. The photomicrograph of the biopsy is shown in figure 4B.

A clinical diagnosis of bronchogenic carcinoma was made.

The patient had subsequently received courses of roentgen therapy with slight improvement.

Comment: In this case a clinical impression had been made of interlobar empyema and the aspiration lung biopsy proved the lesion to be a solid lung tumor.

Case 4: C. W. W., a 63 year old woman, entered the Clinic with a history of a palpable goiter of twenty-five years' duration, symptoms of intermittent hyperthyroidism of ten to twelve years' duration, and a chronic nonproductive cough of two months' duration.

The general physical examination revealed an enlarged modular goiter, with abnormal signs in the right chest. There was dullness over the right lung posteriorly in the level of the eighth to tenth vertebral spine, with decreased to absent breath sounds over this region and a few fine moist râles.

Roentgen examination (Fig. 5A) revealed evidence of a thickened pleura between the right middle and right lower lobes with some degree of effusion. No tumor mass was delineated. The fasting blood cholesterol was 171 mg. per cent, and the basal metabolic rate was plus 18 per cent.

On bronchoscopic examination no direct evidence of tumor was found, although the mediastinum was noticeably greatly thickened and the floor of the right main stem bronchus was pushed upward, as if by a mediastinal mass. No intrinsic lesion was noted.

Aspiration lung biopsy showed masses of tumor cells of variable size with many mitotic figures and atypical nuclear division (Fig. 5B). It had the appearance of carcinoma, and a clinical diagnosis of bronchogenic carcinoma was made.

The patient was advised to have roentgen therapy, which was carried out elsewhere.

Comment: In this patient, no tumor mass was delineated on the roentgenogram, the latter giving a picture of an interlobar effusion. The bronchoscopic examination gave indirect evidence of tumor, the diagnosis being confirmed by aspiration lung biopsy.

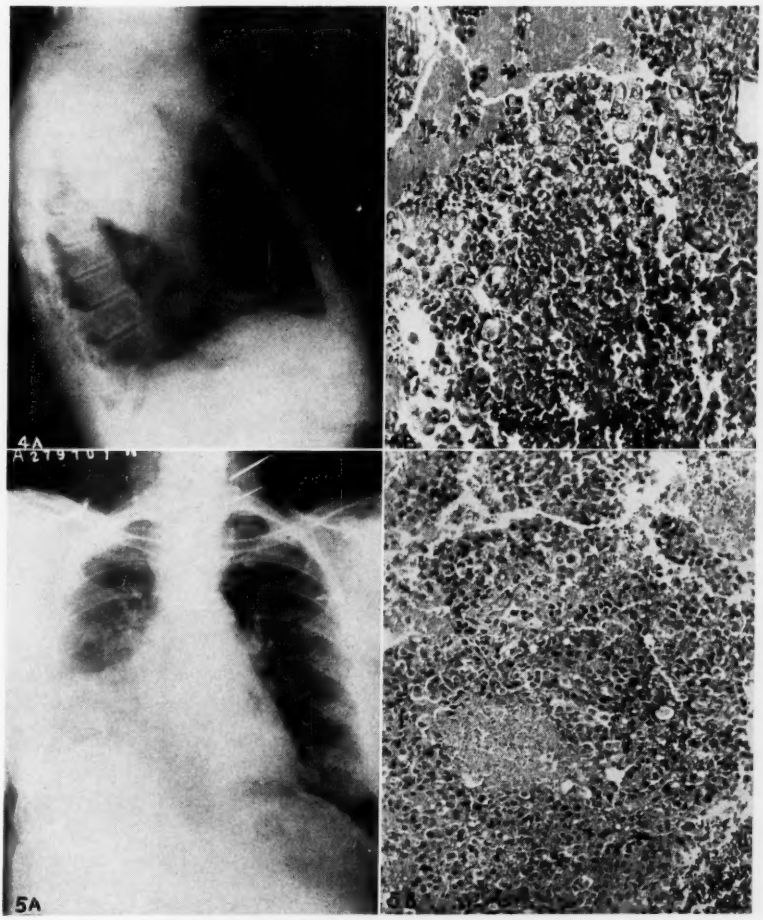

FIGURE 4: A. Lesion suggestive of interlobar empyema as seen in right lateral roentgenogram.

B. Aspiration biopsy revealed solid tumor of bronchogenic type.

FIGURE 5: A. Right lower lobe lesion simulating interlobar effusion with no visible tumor mass.

B. Photomicrograph of aspirated material showing tumor cells of bronchogenic type.

Case 5: P. S., a 21 year old college student was seen on May 18, 1940, with symptoms of a dull pain in the lower right chest anteriorly of five months' duration, and fever and shortness of breath of two weeks' duration. A roentgenogram taken two months previously (Fig. 6A) revealed a fairly circumscribed shadow the size of a grapefruit in the lower right lung. The admission film (Fig. 6B) revealed a massive effusion on the right and the physical signs were entirely those of a total right pleural effusion. The patient's temperature on admission was 101.0°F., and he was quite dyspneic.

On three successive days a total of 5600 cc. of bloody fluid were withdrawn from the right lung by aspiration. Microscopical studies revealed tumor cells (Fig. 6C). The tumor cells were of a highly undifferentiated sarcomatous type suggestive of sympatheticoblastoma. A subsequent surgical biopsy through the anterior chest wall revealed identical cellular structure.

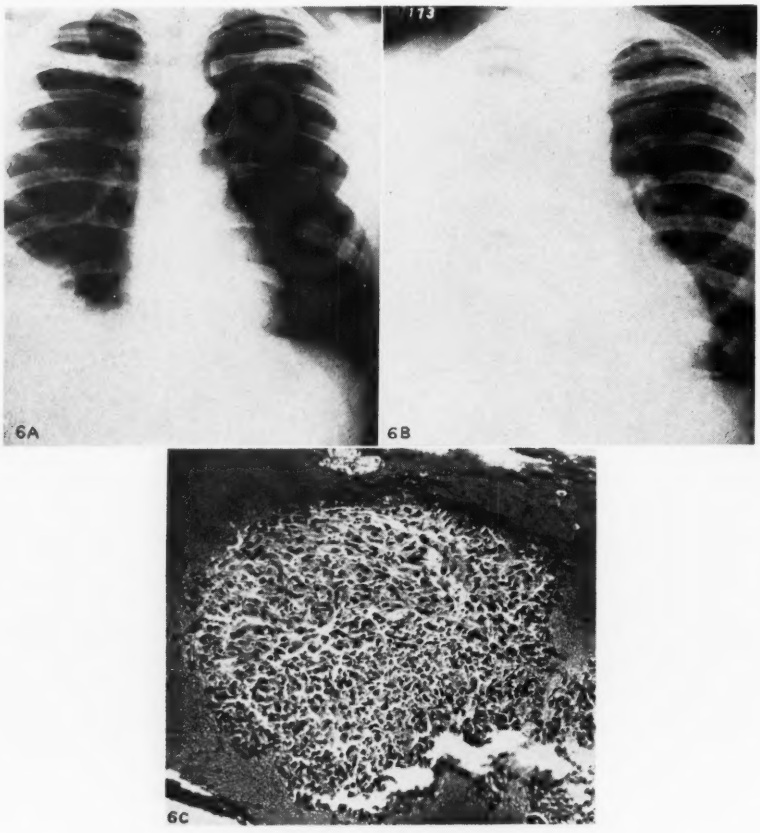

Figure 6: A. Circumscribed lesion seen in lower right chest on films made elsewhere previously.

B. Total right pleural effusion on admission.

C. Tumor cells in bloody pleural fluid (at aspiration biopsy). Microscopically, sympatheticoblastoma.

Under intensive irradiation therapy the patient improved markedly for a time with complete disappearance of the tumor. However, he died nine months later from widespread multiple metastases.

Comment: In this patient the diagnosis was confirmed by the identification of the tumor cells in aspirated pleural fluid.

Case 6: A. B. B., a 46 year old man, was seen on July 16, 1940 referable to pain in the left scapular area radiating to the left arm, of four months' duration.

Physical examination revealed a decreased note over the upper third of the left chest posteriorly, associated with bronchial breathing and increased vocal and tactile

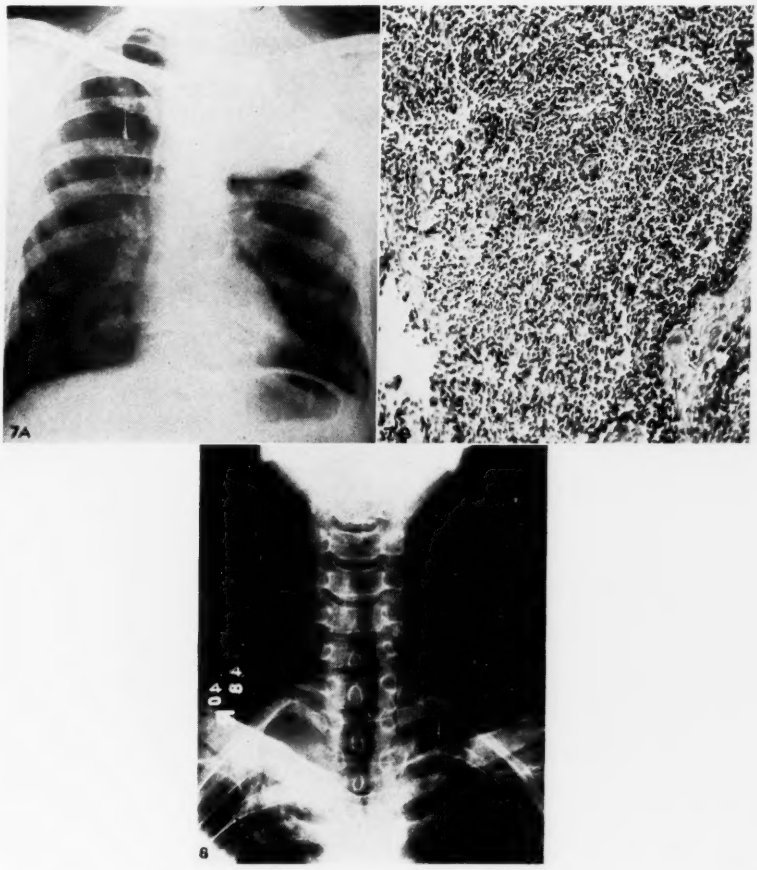

FIGURE 7: A. Circumscribed lesion, upper left lung.
B. Photomicrograph of aspirated material revealing bronchogenic carcinoma.

FIGURE 8: Right superior sulcus tumor with partial destruction of posterior portion of third rib. Aspiration biopsy revealed carcinoma of bronchogenic type.

fremitus. There were a few inspiratory moist râles in the upper left chest anteriorly and in the upper left axilla. A definite left Horner's syndrome was noted. The roentgenogram (Fig. 7A) was interpreted as showing a probable superior sulcus tumor.

Bronchoscopic examination was negative.

The aspiration lung biopsy revealed the presence of carcinoma, as noted in the photomicrograph (Fig. 7B).

In spite of intensive irradiation, he steadily became worse and died one month later. At necropsy, primary carcinoma of the left lung with infiltration of the pleura and thoracic vertebrae, and metastases to the mediastinal nodes and right adrenal were found.

Comment: In this patient the histological appearance of the tumor was demonstrated by aspiration lung biopsy. The lesion was clinically inoperable, as indicated by the presence of the Horner's syndrome.

Case 7: R. L., a 50 year old man, entered the Clinic on December 28, 1940 with symptoms of pain in the right scapular region, radiating down the inner aspect of the right arm, of two months' duration.

The physical examination revealed no significant findings other than the presence of a right Horner's syndrome.

The roentgen examination (Fig. 8) revealed a shadow in the extreme right apex with partial destruction of third posterior rib. The diagnosis was a probable superior sulcus tumor.

Aspiration lung biopsy revealed a definite carcinoma, and a diagnosis of bronchogenic carcinoma of the superior sulcus type was made.

The patient has received palliation to date with no change in the size of the tumor mass on intensive irradiation therapy.

Comment: This patient illustrates the aid of aspiration lung biopsy in microscopic confirmation of an inoperable superior sulcus tumor.

In the two following cases, a diagnosis of metastatic lesions was obtained through aspiration biopsy.

Case 8: E. N., a 52 year old woman, was seen on March 15, 1940 complaining of "chest heaviness" and shortness of breath of three months' duration. A left pleural effusion had been recognized two months previously subsequent to which time six thoracenteses were done with negative findings referable to tuberculosis.

The physical signs were those of a bilateral pleural effusion (Fig. 9A). There was no identifiable parenchymal lesion because of the extensive effusion.

Bronchoscopy revealed negative findings. The aspiration of pleural fluid revealed the presence of probable metastatic malignant cells (Fig. 9B).

The patient died of her disease a few weeks later. At necropsy papillary adenocarcinoma of the left ovary was found with widespread pleural metastases.

Comment: In this case aspiration study was of value in that tumor cells were found in pleural fluid which were identified as not being of primary lung origin.

Case 9: F. E. G., a 56 year old woman, was seen on August 2, 1939 with the chief complaint of recurrent attacks of pain in the upper right quadrant. As a minor symptom she mentioned a dull pain in the upper left chest anteriorly with "soreness in the left side of her neck" of six weeks' duration. The past history was negative. A left mastectomy had been done six years previously, at which time a diagnosis of carcinoma had been made.

The general physical examination was negative, other than the presence of moderate tenderness in the region of the gall bladder. Roentgen examination of the chest revealed a well circumscribed mass in the upper left chest (Fig. 10A). Cholecystography showed a poorly functioning gallbladder with cholelithiasis. Clinical diagnoses of chronic cholecystitis with cholelithiasis and of probably dermoid cyst of the upper left mediastinum were made.

An aspiration lung biopsy was done in the left upper lung field at the second interspace at the level of the junction of the middle and inner third of the clavicle. Thick,

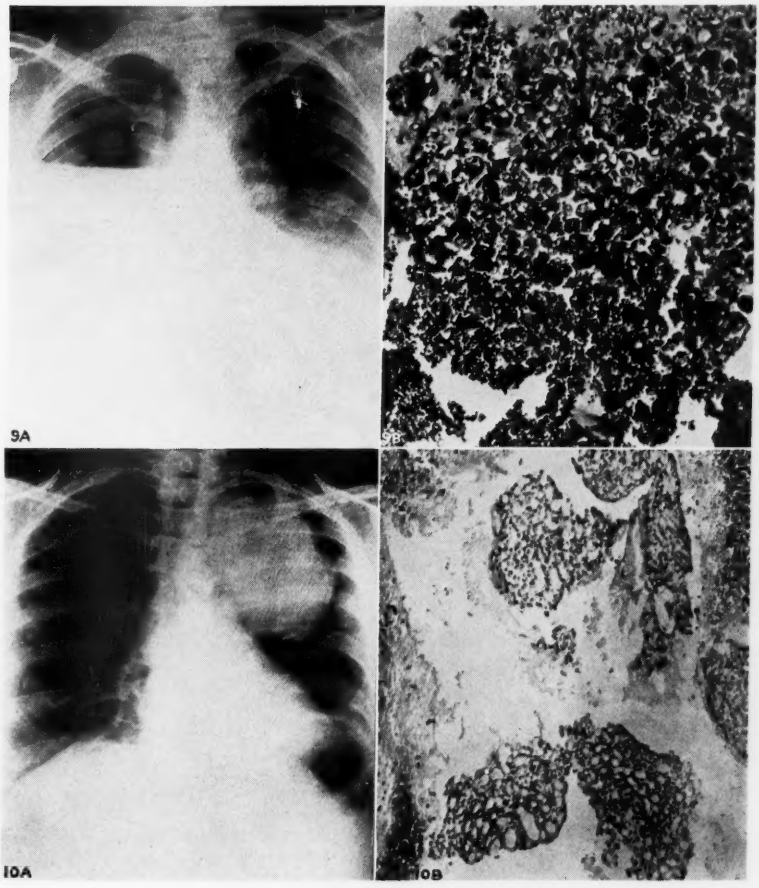

FIGURE 9: A. Bilateral pleural effusion.

B. Aspiration biopsy revealed the pleural fluid to contain metastatic cells. Pleural metastases from papillary adenocarcinoma of left ovary were later found at necropsy

FIGURE 10: A. Solitary circumscribed lesion, left upper lung. Clinical impression; primary carcinoma or dermoid.

B. Aspiration biopsy revealed coil gland carcinoma (identical to slide obtained of breast tumor removed six years previously).

bloody, yellowish-white material was obtained. Microscopic examination (Fig. 10B) revealed masses of small, deeply staining epithelial cells showing some tendency to form tubular or gland-like structures and to form cylindromatous modules. The tumor had the histological characteristics of a coil-gland carcinoma of the breast. On obtaining the slide of the original breast tumor from another hospital, the microscopic appearance was found to be identical.

The patient obtained some palliative improvement on intensive irradiation therapy but died from the metastatic lung lesion six months later.

Comment: In this case a solitary lung tumor on aspiration lung biopsy was found to be a metastatic coil-gland carcinoma and needless lung surgery was prevented.

The two following cases illustrate the aid of aspiration lung biopsy in the diagnosis of inflammatory lesions.

Case 10: R. K., a 46 year old man, was seen on July 20, 1939 with the chief complaint of a persistent cough. He had had lobar pneumonia three months prior to admission, followed by a dry cough, the previous four weeks being associated with profuse mucopurulent sputum and bouts of fever. There was a loss of 50 pounds in weight since the pneumonia. A partial exploratory thoracotomy had been performed elsewhere one month prior to being seen at the Clinic, at which time a presumptive diagnosis of lung tumor had been made.

Upon physical examination the patient was found to be decidedly malnourished. There was limited expansion in the right chest with a dull to flat percussion note on this side posteriorly from the level of the fifth to the ninth thoracic vertebra. Breath sounds were absent in this area and a few crepitant râles were heard in the right midaxillary region.

Roentgen examination of the chest (Fig. 11A) revealed a haziness of the lower half of the right lung which was interpreted as being due to thickened pleura along with parenchymal infiltration. There was no identifiable tumor mass roentgenologically.

Upon bronchoscopic examination no pathology was observed.

Aspiration lung biopsy revealed no tumor tissue. A Type III pneumococcus was found both in the smear and on typing, and a tentative diagnosis of so-called unresolved pneumonia was made.

The patient was sent home for a course of sulfanilamide therapy. He obtained prompt relief of his symptoms and when seen eight months later, the lung was entirely normal clinically and roentgenologically (Fig. 11B).

Comment: In this patient the finding of a type-specific pneumococcus along with negative biopsy for tumor tended to rule out a previous impression of neoplasm and the subsequent course verified the diagnosis of an inflammatory lesion.

Case 11: O. D., a 46 year old colored woman, came to the Clinic on November 1, 1939 with symptoms of the insidious onset of a chronic cough, fever, and dull pain in the anterior left chest, of two months' duration. A previous diagnosis of lung tumor had been made by roentgen examination.

Physical examination revealed decreased percussion notes in the left midlung field over an area of two ribs in width, with a few associated fine crepitant râles. The patient was noted to have a so-called blue-gummed appearance with considerable gingivitis.

Roentgen examination (Fig. 12A) showed a dense, fairly well circumscribed shadow the size of an orange in the anterior axillary line of the left midlung field. No cavity was seen. Repeated sputum examinations were negative for acid-fast organisms and

other pathogens, except for an unusually large number of fusiform and spirochetal types.

Bronchoscopic examination was entirely negative. The left main stem bronchus with its divisions was well visualized and there was no evidence of tumor, nor purulent material.

The aspiration biopsy approach was made anteriorly just midway between the hylum and the peripheral lung zone, no resistance being found on entering the mass, and a large quantity of very foul pus was aspirated. Microscopic examination of the aspirated

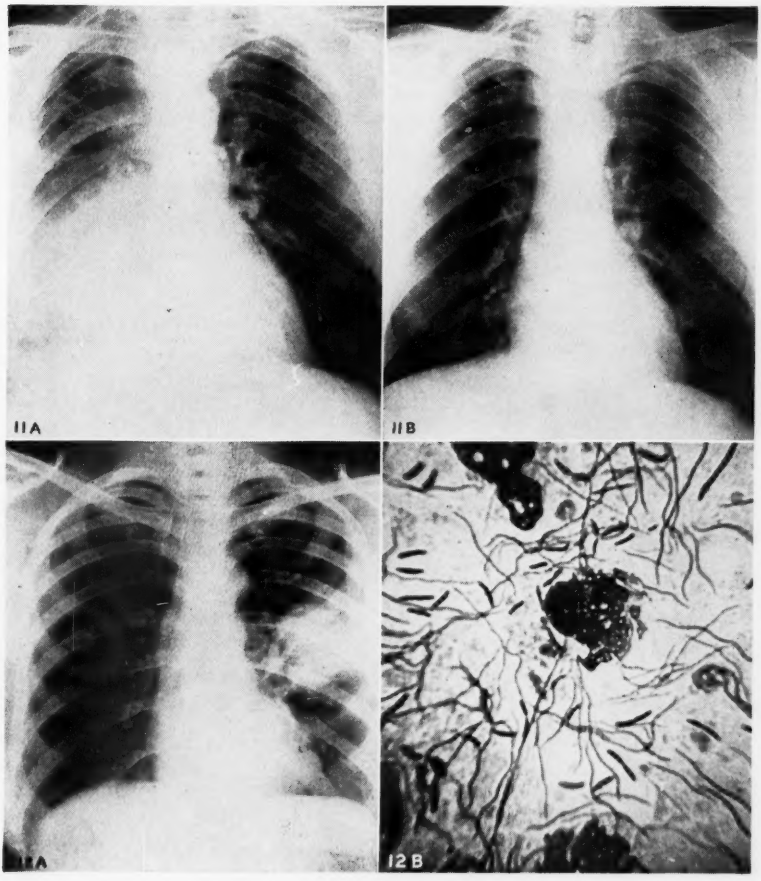

FIGURE 11: A. Lesion, right lower lung. History and previous studies suggestive of bronchogenic carcinoma.

B. Aspiration biopsy negative for tumor cells. Type III pneumococcus isolated. Roentgenogram following chemotherapy.

FIGURE 12: A. Lesion, left lung, referred with clinical impression of tumor.

B. Aspiration revealed typical fusospirochetal lung abscess. Smear of aspirated material reveals fusiform and spirochetal elements of Vincent's group.

material (Fig. 12B) revealed numerous fusiform and spirochetal organisms of the Vincent's type both on the smear and under darkfield examination. A diagnosis of a fusospirochetal lung abscess was made. Surgery was advised but the patient refused this. Marked improvement on medical management occurred in the ten days before leaving the hospital. However, the patient later developed pneumonia and expired.

Comment: In this patient aspiration lung biopsy established a diagnosis of a fusospirochetal lung abscess where a previous tentative diagnosis of lung tumor had been made.

Case 12: D. S., a 51 year old man was referred to the Clinic on May 26, 1941 with the symptoms of cough, dysphagia and weight loss (20 pounds) of four months' duration.

The physical examination revealed a decreased note in the upper right lung adjacent to the mediastinum. The roentgen examination of the chest outlined a fairly

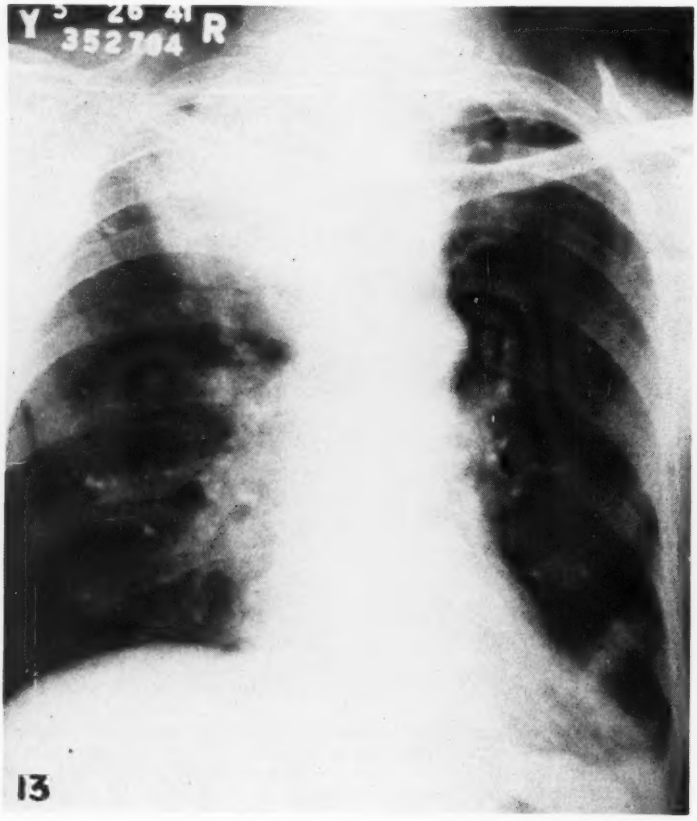

Figure 13: Lesion of right upper lung. Aspiration biopsy revealed squamous cell bronchogenic carcinoma.

smooth mass in the upper right lung adjacent to the mediastinum as seen in figure 13. An esophogram was normal except for displacement to the left and anterior by the extrinsic lesion.

Bronchoscopy showed some degree of tracheal fixation but did not visualize the lesion.

Aspiration biopsy was made, the needle being inserted in the right second posterior interspace and the diagnosis of squamous cell bronchogenic carcinoma established microscopically. The lesion was concluded to be inoperable clinically because of the tracheal fixation, and roentgen therapy was advised.

Comment: This patient illustrates the frequent upper lobe primary lung tumor where tissue for biopsy is often unobtainable bronchoscopically (this being due to mechanical difficulty in seeing beyond the upper lobe orifice with the instrument).

SUMMARY

Aspiration biopsy is often a very helpful diagnostic procedure in patients exhibiting roentgenologic disease of the bronchopulmonary tract or pleura where other measures fail. It is of value in certain inflammatory lesions, as well as in primary or metastatic neoplasms.

When done with care, aspiration biopsy is a simple and relatively safe procedure. When indicated, its value exceeds its risk. The technic, with the instrument used, is described and a series of 12 illustrative cases are presented.

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THE PROGNOSIS OF RHEMATOID ARTHRITIS

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Rheumatoid arthritis presents a difficult and often a discouraging problem. Because the etiologic factors are unknown, the prognosis is questionable, and in viewof the complexity of the problem and often the slow response to therapy, the attitude generally is pessimistic and no definite attempt is made to help these unfortunate individuals. Every gradation of involvement is observed, and each patient presents an individual problem of prognosis. In the earliest stages of migrating pains without any objective signs of rheumatoid arthritis, the course of the disease is questionable. In other cases with severe deformities or complete ankylosis, the prognosis is poor.

The problem is how to obtain information from these patients which might be used as a guide in making a reasonable prognosis. The first prerequisite is a detailed history, including information regarding the onset and course of the disease, previous infections, the home and occupational environment, mental attitude of the patient, and heredity factors. Other factors which often precede the onset of rheumatoid arthritis are chronic exhaustion, exposure to cold, psychic trauma, pregnancy, psoriasis, hyperthyroidism, coronary thrombosis, and major operations.

Second in importance is a thorough physical examination, including examination of the involved joints and of the general stature and body mechanics. A thorough search should be made for foci of infection, the most common sources of which are the teeth, tonsils, sinuses, prostate pelvis and gallbladder. Roentgenographic study of a typically involved joint indicates the cartilaginous and bony involvement.

Certain laboratory studies give essential information about the patient's general condition. The routine blood examination determines the degree of secondary anemia which is often present. Estimation of the sedimentation rate gives a fair index of the amount of activity in the joints or body. The glucose tolerance test often presents information worthwhile to warrant its use, as we have observed that many patients have poor utilization of sugar. The blood uric acid determination is done routinely to exclude the possibility of gout in questionable cases. As a lowered metabolic rate is observed in a very large number of cases, the basal metabolism should be checked. Anacidity and hypo-acidity also are not uncommon findings. A questionable involvement of the sinuses should be studied roentgenographically. Roentgenograms of the teeth also should be made to eliminate the possibility of apical infection. If gastrointestinal disturbances, particularly gallbladder symptoms, are present, complete roentgenographic studies should be undertaken.

From these examinations information may be obtained to use in making a prognosis, which should be based not only upon the physical examination and laboratory studies, but also upon the patient's general condition. If the patient has the will and determination to get well, some of the treatment has been accomplished.

Another very vital factor in the prognosis is whether or not the treatment can be adequate. The best results are usually obtained from complete bed rest in the hospital. Unfortunately, this is not possible in many instances, and consequently the patient often receives inefficient or ineffective therapy.

We are all aware of the fact that there are many methods for treating rheumatoid arthritis. Complete bed rest for both mental and physical relaxation is one of the first essentials. Many patients suffer from fatigue and exhaustion, and worry about deformities from progression of the disease. If the patient can be hospitalized and daily active treatment instituted, the patient's outlook often is improved. Environmental change is another beneficial measure. Muscular relaxation should be obtained. While the patient is in bed, he should have joint use to prevent stiffening and contracture by carrying each joint through complete range of motion one or more times each day.

The secondary anemia so characteristic of this disease usually does not respond satisfactorily to iron therapy alone. To restore the blood to a normal level, blood transfusions should be given in adequate numbers to obtain a normal blood picture. If a severe anemia is present, four or five transfusions may be necessary. In addition to restoring a normal blood picture, a nonspecific reaction is frequently obtained which is most beneficial.

Dietary treatment is a disputed question. However, we know there is a metabolic disturbance from the study of glucose tolerance curves. The blood sugar at the first and second hours very often is higher than normal, but usually reaches normal, however, at the end of the fourth hour. Because of this poor utilization, the low carbohydrate diet is used unless the patient is markedly underweight and emaciated. Often these patients have been on a poorly balanced diet. The low carbohydrate diet contains adequate protective foods and proteins with sufficient calories, as follows:

HIGH VITAMIN—LOW CARBOHYDRATE DIET

1. A liberal portion each day of any fresh fish, meat or fowl.
2. One or two eggs each day.
3. Fresh vegetables, both raw and cooked, as follows:

(a) Two fresh raw vegetables from the following: (May be taken in salad form)

Cabbage	Swiss Chard	Pepper
Lettuce	Cucumber	Carrot
Tomato	Radish	Onion
Endive	Celery	Water Cress

(b) At least two fresh cooked vegetables from the following:

Asparagus	Brussel's Sprouts	Beets
Egg plant	Mushrooms	Kale
String beans	Tomato	Spinach
Cabbage	Peas	Cauliflower
Onion	Broccoli	Parsnips
Turnips	Kohlrabi	
Celery	Squash	
Rhubarb	Carrots	

4. Fruit, especially fresh fruit in season, liberally each day. It is best to eat fruits in place of made desserts and pastries; oranges, grapefruit, pears, pineapple, melon, berries, and apples are especially good. Use just sufficient sugar to make the fruit palatable.
5. Two glassfuls of milk or buttermilk each day. Other beverages with a minimum of sweetening may be added.
6. No cereal nor bread, except two slices of whole wheat bread daily.
7. Butter, cream and salad dressing as desired.
8. Nuts as desired.
9. Add vitamins as follows (unless otherwise directed):
   (a) Wheat germ for Vitamin B. Take two tablespoonfuls each day
   (b) Fresh yeast for Vitamin B. Two cakes each day.
   (c) Cod liver oil for Vitamins A and D, two tablespoonfuls, twice a day or an adequate amount of one of the newer fish oils.
10. Avoid the following:

    All vegetables not on list

    All bread and bread substitutes, except the allowed whole wheat bread

    All cereals

    All desserts such as puddings, cookies, pies, cake, pastry and ice cream

    All very sweet fresh fruits and all dried fruits such as figs, dates, raisins and prunes, unless taken only occasionally in small amounts

All spaghetti, noodles, macaroni, rice, candy, honey, syrups, jellies

All sugars except such as are necesssry to make food and drink palatable.

When the atypical blood sugar curve is obtained, ten units of protamine-zinc insulin are given daily, usually for a period of from four to six weeks.

Nutritional deficiency often plays a part in the etiology, and adequate vitamins should be added to the diet. This deficiency certainly is not the cause of the disease, but may be an important influencing factor. Cod liver oil given in ounce doses twice a day is most valuable. Wheat germ and yeast are excellent sources for vitamin B. If these vitamins are not well tolerated by the patient, the concentrated forms may be substituted in adequate dosage.

The removal of infected foci probably will not cure arthritis, but very often will improve the general health. It is unwise to remove teeth which are only suspected, as this often leaves the patient without adequate masticating surface and prevents proper nutrition. Focal infection is probably an influencing factor and should be removed as soon as possible. Focal infection probably is more important early in the course of the disease than later. If the patient is markedly debilitated or is having an acute exacerbation, operative procedures should be used with caution as they often increase joint involvement and cause exacerbation of symptoms.

The value of many drugs recommended in the treatment of this disease has been questioned and in many instances only serve to relieve pain. As many of these patients have achlorhydria or hypochlorhydria, dilute hydrochloric acid should be given. If the metabolism is low, thyroid extract should be added. Iron in the form of Blaud's mass often is of value even if the anemia has been corrected with blood transfusions.

Arsenic in some form often is beneficial and can readily be administered in the form of neoarsphenamine in doses of 0.3 gm. twice weekly for six to eight injections.

An important adjunct to the treatment of these patients is the use of nonspecific vaccine, such as the stock typhoid-paratyphoid vaccine. For the first treatment 25 million bacteria are injected intravenously. Each succeeding injection is given after 24 hours of normal temperature. The amount injected each time is twice the number of bacteria given at the preceding dose. The temperature reaction following the first injection usually lasts longer than 48 hours, so 72 hours should elapse between the first and second dose. As the succeeding injections are less prolonged, the third and succeeding doses usually can be given at 48-hour intervals. Nonspecific protein therapy should not be given

to seriously ill patients, but should be reserved for use as an aid when the patient is improving and on the upgrade. Three to six injections are given.

Another important adjunct is physical therapy. The patient with arthritis usually requires treatment over a long period of time and simple physical methods of treatment should be employed. Short wave diathermy is not a necessity, but if it is available, it should be used especially for treating the larger joints such as the shoulder, back, hips, and knees. The local application of heat increases circulation and tissue metabolism in the involved part, and a sedative effect also is obtained. In an acute rheumatic joint, the first application of short wave diathermy should be at low intensity and for a period of time shorter than the usual treatment. When there is congestion in a joint, added excess heat may increase the congestion and intensify the symptoms. Treatments can be given every day if the patient is in the hospital, and every other day if the patient is an out-patient. In addition to local heat, the systemic application of heat is of value in increasing circulation and metabolism. This is especially true when many joints are involved and they cannot all be treated locally. If at home, the patient can apply heat daily from an infra-red generator or the paraffin bath which is especially suitable for the hands.

The electrically controlled paraffin bath gives an excellent form of heat, especially for the hands and feet. The application of daily treatment for the hands can be easily done by the patient at home. The following are directions for use:

Fill the top part of a large double boiler (6 quart) with paraffin (6 to 8 pounds) and the lower part with hot water. Heat until almost all the paraffin is melted, but be sure an unmelted piece remains. This is important if burns are to be avoided. Remove from the fire, leaving the water in the bottom of boiler.

Dip the hand quickly into the paraffin, keeping the fingers separated and being careful not to touch the sides or bottom of the boiler. Remove the hand from the boiler until the paraffin hardens on the hand, then dip and quickly remove again. Repeat this procedure until a thick "glove" is formed, after which the hand is kept immersed in the paraffin for ten minutes to half an hour. Peel off the glove and put the paraffin back into the boiler.

Massage must be given at frequent intervals, and should follow the application of heat. This also can be done at home by some interested member of the family who has received instruction in the procedure. Heavy massage over an arthritic joint may cause a marked local reaction. Therefore, the prescription for this should be made specific by the physician.

During the acute phase, rest in proper supports is important. Passive manipulation should be avoided because it may increase swelling and interfere with the circulation which already is poor. Sunbaths from the natural source should be taken whenever possible, and the ultra-violet lamp should be used in the winter.

Patients with rheumatoid arthritis improve in a hot dry climate if a prolonged stay is possible. Climate alone, however, is of little benefit as it is only an aid in treatment and not a substitute for other therapy. Often a patient sent to the southwest without supervision obtains no results because climate alone may not be depended upon for improvement.

Every patient with rheumatoid arthritis should be under orthopedic supervision from the beginning of treatment in order to prevent contractures. With proper splinting and proper care, contractures usually can be avoided. If a contracture develops after the disease has run its acute course, it can often be corrected by orthopedic care and the joint returned to usefulness.

The following case report illustrates some of the points discussed above.

Case 1: A 47 year old executive was first seen in August, 1939. He gave a history of swollen and painful joints since February, 1939, following an attack of influenza. First the hands and later the knees, ankles, toes and shoulders had been involved. Fatigue had developed along with weakness, and he had lost twenty pounds in weight. He was bed-ridden.

Physical examination revealed the weight to be 130 pounds, the temperature 100° F. and the blood pressure 130 mm. systolic and 85 mm. diastolic. The general stature was of the hyposthenic type, and the patient was quite pale. Transillumination revealed the sinuses to be clear. The tonsils were present, and purulent material could be expressed from the left tonsil. Roentgen examination of the teeth revealed one questionable tooth with some evidence of periapical involvement. A devitalized tooth had been removed four months before admission and had caused severe exacerbation of symptoms. Examination of the lungs, heart, and abdomen revealed no abnormal findings. The prostate gland was normal. Examination of the joints showed marked involvement in the fingers, wrists, elbows, shoulders, knees and ankles with limitation of movement and considerable inflammation and swelling.

General laboratory studies revealed a normal urinalysis. Examination of the blood showed 4,080,000 red cells with 70 per cent hemoglobin, and there were 6,200 white cells. The sedimentation rate was 1.9 mm. per minute (the high normal of the O'Rourke-Ernstene method used at the Clinic is 0.45 mm.). The uric acid was 2.2 mg. per 100 cc. Wassermann and Kahn tests of the blood gave negative reactions. The basal metabolic rate was plus 1 per cent. The Ewald test meal showed a free acid of 20 and a total acid of 40 degrees. The glucose tolerance curve showed the fasting blood sugar to be 84 mg. per 100 cc.; in one hour it was 219 mg. (high normal 200). In two hours the blood sugar was 222 mg. per 100 cc. (high normal 150 mg.). The third hour blood sugar level was 170 mg. per 100 cc. (normal 120 mg.). At the fourth hour the level was within normal limits. The chest roentgenograms were normal. Roentgenograms of the intestinal tract showed a normally functioning gallbladder without calculi, and the stomach, duodenum and colon were normal. Roentgenograms of the kidneys, ureters, and bladder showed no suspicious urinary tract shadows. A roentgenogram of the right hand revealed marked demineralization of the bones of the hand and wrist. There were no changes in the joint cartilages.

This patient presented the typical picture of very active rheumatoid arthritis involving many joints, and running a rapid course. He received two blood transfusions of 500 cc. each. Neoarsphenamine, 0.3 gm., was given intravenously twice weekly. A low carbohydrate, high vitamin diet was given. One ounce of cod liver oil twice daily, a cake of fresh yeast with each meal, and two Brewer's yeast tablets three times daily were taken. Protamine-zinc insulin, 10 units daily, was given. Physical therapy was applied in the form of diathermy and massage to the knees, and quadriceps exercises. The hands were treated in the hand paraffin bath, followed by massage. The infra-red baker was applied to the knees and feet for one hour three times daily.

The patient had definite reactions to the neoarsphenamine with generalized aching and some fever. After the fourth injection he had a marked reaction with a chill, and the temperature rose to 104°F. Following this episode the temperature fluctuation was less and there was only a slight daily rise. Five days later one injection of neoarsphenamine, 0.15 gm., was given.

After twenty-four days in the hospital on the above mentioned treatment the patient had less pain with some general improvement. It was then felt advisable to give a course of nonspecific vaccine therapy, in the form of typhoid vaccine. Following this he was discharged from the hospital, generally improved. Considerably less activity was present in the joints, with little pain. The patient could walk with assistance. He continued with the diet, vitamins and iron. He also received physical therapy three times weekly to the affected joints.

Three weeks after discharge from the hospital the hemoglobin dropped to 71 per cent and he was given two blood transfusions of 500 cc. each. He then went to Florida for the winter, continuing with the medication and local therapy. In May, 1940 the devitalized tooth was removed. He continued to improve and was able to replace his crutches by a cane. With the use of exercise apparatus such as a stationary bicycle, muscle tone in the legs increased and the ankles became stronger. Examination of the blood in November, 1940 showed 4,910,000 red cells with 89 per cent hemoglobin. He again went to Florida for the winter and plans to resume his former occupation upon his return.

This patient was able to have adequate treatment, and cooperated to the fullest extent. If this patient had not had active treatment nor the will to get well, he probably would have been an invalid. Of course, such an excellent result cannot be obtained in every patient. Some are not benefited by any treatment and a milder case may recover without any treatment. However, every patient should have the benefit of active treatment.

The following case illustrates the findings and the treatment in early rheumatoid arthritis.

Case 2: This patient was a 24 year old nurse who had a complete physical examination in September 1940, at which time there were no abnormal findings. In April 1940, soreness developed in the feet and hips, followed by pain and swelling in various joints of the body, especially in the knees, wrists, elbows and sternoclavicular joint.

The only important laboratory finding was a blood count of 4,230,000 red cells with 61 per cent hemoglobin. Three blood transfusions of 500 cc. each were given. She was placed on a low carbohydrate, high vitamin diet, Blaud's mass, grains 20, three times daily; and neoarsphenamine, 0.3 grains, twice weekly for six injections. Local therapy consisted chiefly of the use of the hand paraffin bath, and massage of the feet and hands; infra-red baking was applied to the knees. She was kept at rest and in May, six weeks later, the joint involvement had subsided completely. She rested for the remainder of the month, during which time she took sun baths. She now has returned to her occupation.

This patient received early active treatment which was followed by a rapid response. There, of course, is always the possibility of a recurrence; nevertheless, the active treatment brought the symptoms under control.

CONCLUSIONS

After a complete study, information is available to help in making a prognosis in rheumatoid arthritis. In some instances, however, the prognosis will be a difficult problem.

Results depend upon the severity and stage of the disease and the extent of joint damage at the time treatment is begun.

With adequate treatment many of the early cases will recover; later, the disease may be arrested and most patients restored to a comfortable and useful life.